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# BLOOD SUGAR METABOLISM IN CERTAIN DERMATOSES

## WITH SPECIAL REFERENCE TO ACNE VULGARIS

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In a recent paper Strickler and Saylor [1] reported the results of a preliminary investigation of blood sugar in acne vulgaris. In all the eighty-seven determinations made by them, there were only 10 per cent showing hyperglycemia, and the conclusions drawn were that hyperglycemia could not be said to characterize acne, nor did any relation appear to exist between changes in the blood sugar and the course of the disease. Although reports of numerous investigators are not in close agreement, the idea that blood sugar and acne are related seems as yet to be accepted in many quarters. The suggestion has frequently been made that the blood sugar in acne may vary periodically, following more or less regularly periods of activity and remission. Although this latter conception seems highly improbable, yet it is possible that single determinations made on groups of patients could have led to erroneous conclusions.

To investigate the various factors that might affect the blood sugar level and its relation to the course of acne, Strickler and Saylor [1] undertook multiple determinations over periods as long as three months. They found that in numerous instances the blood sugar on a restricted diet could increase or decrease, but that the patient in both instances could show clinical improvement. Because the number of cases reported by Strickler and Saylor were relatively small, it was decided to extend the investigation to cover more cases and again to correlate the findings with the clinical picture.

The present investigation is, therefore, a repetition of the general outlines of the work of the foregoing investigators extended to cover a larger number of cases in an attempt to arrive at a definite conclusion

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1. Strickler, A., and Saylor, M. A.: Sugar Metabolism in Acne Vulgaris, Arch. Dermat. & Syph. **20**:705 (Nov.) 1929.

on several points on which there appears to be considerable disagreement. Particular attention has been given to the following: (1) the percentage of cases of acne showing hyperglycemia; (2) whether the amount of blood sugar varies with clinical improvement or relapse, and (3) whether particular types of acne are characterized by hyperglycemia.

## PLAN OF INVESTIGATION

In all the cases reported no attempt has been made to select on the basis of mildness or severity. As many determinations as possible were made on each patient. Each patient was instructed to present himself for blood tests without breakfast, and the determinations were carried out within three hours after drawing of the blood. By an unregulated or unrestricted diet is meant that the patient was not committed by habit to any single diet such as vegetable, meaty, etc. All patients, however, were instructed to avoid excessive sugar, candies, pastry, etc.

The Folin-Wu method [2] was used throughout. The normal range of blood sugar was taken as from 80 to 110 mg. per hundred cubic centimeters.

## ACNE VULGARIS

*Review of the Literature.*—Levin and Kahn [3] were among the first to study the blood sugar in acne vulgaris. In their report of fifteen cases of acne six readings were above 100 mg. Schamberg and Brown [4] reported the blood sugar in twenty-five cases of acne to be normal, and they stated specifically that they had not observed the hyperglycemia that various writers claimed existed in acne. McGlasson [5] determined the blood sugar in a wide variety of skin diseases and reported that from 91 to 96 per cent of the cases had values above 110 mg. Schwartz, Heimann and Malinkin [6] placed various skin diseases in two groups: (1) those in which hyperglycemia is frequent, such as acne, seborrhea and sycosis, and (2) those in which hyperglycemia is rare. They suggested that there appears to be a selective force causing association between diseases of the pilosebaceous follicles and excess of blood sugar. Greenbaum [7] has recently examined patients with acne for

2. Hawk and Bergeim: Practical Physiological Chemistry, ed. 9, Philadelphia, P. Blakiston's Son & Company, 1927, p. 381.

3. Levin, O. L., and Kahn, Max: The Chemistry of the Body in Diseases of the Skin, Am. J. M. Sc. **162**:698, 1921.

4. Schamberg, J. F., and Brown, H.: The Chemistry of the Blood in Diseases of the Skin, Arch. Dermat. & Syph. **21**:1 (Jan.) 1930.

5. McGlasson, I. L.: Hyperglycemia as an Etiologic Factor in Certain Dermatoses, Arch. Dermat. & Syph. **8**:665 (Nov.) 1923.

6. Schwartz, H. J.; Heimann, W. J., and Malinkin, H. C.: Sugar Content of the Blood in Various Diseases of the Skin, J. Cutan. Dis. **34**:159, 1916.

7. Greenbaum, S. S.: Tolerance for Dextrose in Acne Vulgaris, Arch. Dermat. & Syph. **23**:1064 (June) 1931.

dextrose tolerance. An examination of thirty-nine patients with acne and of fifteen patients without acne revealed so little difference in dextrose tolerance that he was unwilling to base any conclusion on it.

*Comment.*—Tables 1 and 1A record the results of blood sugar determinations in 101 cases of acne. The tabulations are subdivided, table 1 giving the results of multiple determinations and table 1A of single determinations. In table 1 the abbreviations in the column "Predominating Type of Lesion" are used as follows: Pu, indicates pustular; Pa, papular; Com, comedones; Seb, sebaceous, and Hyp, hyperphysiologic. In all cases the predominating type of lesion was chosen as descriptive. The various types of lesions are distributed as follows: Pu, 41 per cent; Com, 21 per cent; Pa, 15 per cent; Seb, 13 per cent, and others, 10 per cent.

Of ten cases on which four determinations were made over a period of from two to three months, six, or 60 per cent, showed a regular increase in the blood sugar; one, or 10 per cent, a rather sharp rise with a subsequent decline, and three, or 30 per cent, relatively little change.

Of twenty-eight cases on which three determinations were made, six, or 21 per cent, showed a regular increase to a maximum; five, or 18 per cent, showed a rather sharp rise with a subsequent falling off; five, or 18 per cent, showed a more or less sharp decrease from a high to a low blood sugar, and twelve, or 43 per cent, were either irregular or changed relatively little.

Obviously, the foregoing statements cannot be made concerning cases on which less than three determinations have been made. However, an examination of those cases on which two or more determinations have been made reveals that there is no relation between the blood sugar and the course of the disease. The cases selected to illustrate this point are cases 1461 and 1874. The patient in case 1461 showed improvement when the blood sugar rose from 78 to 130 mg. and had a relapse when the blood sugar fell to 93 mg. The patient in case 1874 improved when the blood sugar fell from 105 to 82 mg. and had a relation between the blood sugar and the age, sex, duration of the disease relation between the blood sugar and the age, sex, duration of the disease or the type of lesion.

The total number of determinations recorded in tables 1 and 1 A is 202. Of these 202 examinations, 20, or 9.9 per cent, gave values above 110 mg. Based on the number of patients rather than on the number of determinations, it would appear that of the 101 cases, 19, or 18.8 per cent, at some time during the period of observation exhibited an increase in blood sugar over 110 mg. However, in no instance in which 3 or 4 determinations were made did the level of the blood sugar constantly remain above 110 mg., nor was the elevation consistently

TABLE 1.—*Multiple Blood Sugar Determinations in Fifty-Seven Cases of Acne Vulgaris*

| Case | Age | Sex | Predominating Type of Lesion* | Duration, Yr. | Blood Sugar, Mg. per 100 Cc. | Date of Determination | Clinical Observations | Diet and Comment |
|---|---|---|---|---|---|---|---|---|
| 1398 | .. | F | Pa | 3 | 93 | 8/ 8/30 | Very few papules | Vegetable |
| | | | | | 82 | 9/ 5/30 | Improving | |
| | | | | | 93 | 10/ 1/30 | Improving | |
| | | | | | 103 | 10/18/30 | Stationary | |
| 563 | 16 | M | Seb | 1 | 82 | 7/15/30 | ..... | Abundant starch; no sweets or fried foods |
| | | | | | 96 | 8/22/30 | Improving | |
| | | | | | 107 | 10/11/30 | Improving | |
| | | | | | 114 | 10/25/30 | Stationary | |
| 1709 | 24 | M | Pa | 6 | 80 | 7/19/30 | Numerous inflamed papules | Health good |
| | | | | | 76 | 8/18/30 | Improving | |
| | | | | | 95 | 9/10/30 | Stationary | |
| | | | | | 94 | 10/10/30 | Improving | |
| 1641 | 34 | F | Seb | 20 | 84 | 7/19/30 | Numerous lesions and pustules | Not aggravated by menses |
| | | | | | 91 | 9/ 8/30 | Improved | |
| | | | | | 86 | 10/ 8/30 | Stationary | |
| | | | | | 108 | 10/18/30 | Improving | |
| 1841 | 20 | M | Pu | 5 | 95 | 7/19/30 | Improving | Careful of diet; chronic constipation and indigestion |
| | | | | | 97 | 8/13/30 | Improving | |
| | | | | | 99 | 9/10/30 | Few new papules | |
| | | | | | 103 | 10/ 3/30 | Improving | |
| 1971 | 30 | M | Pu | 5 | 106 | 7/23/30 | Stationary | |
| | | | | | 100 | 8/18/30 | Aggravated | |
| | | | | | 107 | 9/ 8/30 | Improving | |
| | | | | | 93 | 10/ 3/30 | Stationary | |
| 1968 | 19 | M | Pu | 3 | 98 | 7/23/30 | Pustules numerous | Unregulated diet; no digestive disorders |
| | | | | | 112 | 8/20/30 | Improving | |
| | | | | | 106 | 9/19/30 | Stationary | |
| | | | | | 95 | 10/18/30 | Improving | |
| 1347 | 20 | M | Pu | 4 | 83 | 7/25/30 | Improving | Health good; no digestive disorders |
| | | | | | 88 | 8/18/30 | Improving | |
| | | | | | 96 | 9/ 8/30 | Improving | |
| | | | | | 101 | 10/ 1/30 | Stationary | |
| 1100 | .. | .. | .... | .. | 92 | 7/25/30 | | |
| | | | | | 95 | 8/20/30 | | |
| | | | | | 98 | 9/12/30 | | |
| | | | | | 87 | 10/ 8/30 | | |
| 414 | 22 | F | Pa | 1 | 79 | 8/ 6/30 | Improving | |
| | | | | | 103 | 8/27/30 | No active lesions | |
| | | | | | 114 | 9/17/30 | Stationary | |
| 141 | 35 | F | Pa | 21 | 84 | 8/16/30 | Improving | Aggravated by menses |
| | | | | | 76 | 10/ 1/30 | Improving | |
| | | | | | 102 | 11/15/30 | Stationary | |
| 1120 | 24 | F | Pa | 8 | 87 | 8/16/30 | Improving | Unregulated diet |
| | | | | | 94 | 9/13/30 | Improving | |
| | | | | | 97 | 10/25/30 | Stationary | |
| 1437 | 21 | F | Seb | 1 | 87 | 8/22/30 | Improving | |
| | | | | | 101 | 9/12/30 | Improving | |
| | | | | | 97 | 10/18/30 | Stationary | |
| 2156 | 22 | F | Pu | 4 | 89 | 9/ 6/30 | Improving | Careful of diet; aggravated by menses |
| | | | | | 94 | 10/ 1/30 | Aggravated | |
| | | | | | 95 | 11/15/30 | Improving | |
| 2179 | 21 | F | Pu | 2 | 114 | 9/12/30 | Stationary | Unregulated diet; chronic constipation |
| | | | | | 108 | 10/ 8/30 | Improving | |
| | | | | | 106 | 11/15/30 | Improving | |
| 2040 | 23 | F | Com | 2 | 82 | 8/ 8/30 | Stationary | Unregulated diet; not aggravated by menses |
| | | | | | 89 | 9/ 3/30 | Improving | |
| 1962 | 19 | M | Seb | 3 | 105 | 8/13/30 | Stationary | |
| | | | | | 81 | 10/ 1/30 | Stationary | |

* In this column, Pu indicates pustular; Pa, papular; Com, comedones; Seb, sebaceous, and Hyp, hyperphysiologic.

TABLE 1.—*Multiple Blood Sugar Determinations in Fifty-Seven Cases of Acne Vulgaris—Continued*

| Case | Age | Sex | Predominating Type of Lesion* | Duration, Yr. | Blood Sugar, Mg. per 100 Cc. | Date of Determination | Clinical Observations | Diet and Comment |
|---|---|---|---|---|---|---|---|---|
| 1380 | 17 | M | Pa | 3 | 97 | 8/13/30 | Improving | |
| | | | | | 124 | 9/12/30 | Improving | |
| 21 | 18 | F | Pu | 3 | 85 | 8/15/30 | Aggravated | |
| | | | | | 104 | 10/ 1/30 | Improving | |
| 1708 | 18 | F | Hyp | 3 | 108 | 9/ 6/30 | Stationary | |
| | | | | | 89 | 10/ 5/30 | Stationary | |
| 2219 | 15 | M | Pu | 3 | 114 | 9/19/30 | Improving | Regulated diet; no digestive disorders |
| | | | | | 101 | 10/ 8/30 | Few new pustules | |
| | | | | | 97 | 11/12/30 | Stationary | |
| 2220 | 17 | M | Pu | 2 | 103 | 9/19/30 | Stationary | Unregulated diet; chronic constipation |
| | | | | | 98 | 11/ 8/30 | Improving | |
| | | | | | 108 | 12/ 6/30 | Stationary | |
| 2045 | 21 | F | Pu | 6 | 98 | 8/ 9/30 | No new lesions | Unregulated diet; constipation; acne aggravated by menses |
| | | | | | 99 | 9/13/30 | Improving | |
| | | | | | 89 | 10/11/30 | Much improved | |
| 1059 | 17 | F | Pu | 2 | 95 | 8/13/30 | Improving | Eats fats, sweets abundantly; aggravated by menses |
| | | | | | 117 | 9/12/30 | Improving | |
| | | | | | 108 | 10/11/30 | Stationary | |
| 1901 | 16 | M | Pu | 3 | 93 | 8/13/30 | Aggravated; spreading | Unregulated diet |
| | | | | | 88 | 9/ 5/30 | Stationary | |
| | | | | | 97 | 10/10/30 | Aggravated | |
| 1994 | 20 | M | Pu | 2 | 94 | 8/23/30 | Aggravated | |
| | | | | | 94 | 9/27/30 | Improving | |
| | | | | | 108 | 10/25/30 | Improving | |
| 1414 | 19 | M | Pa | 2 | 158 | 8/25/30 | Improving | Unregulated diet |
| | | | | | 114 | 9/20/30 | Stationary | |
| | | | | | 97 | 11/26/30 | Stationary | |
| 944 | 18 | M | Pa | 3 | 85 | 8/27/30 | Aggravated | |
| | | | Com | | 78 | 9/17/30 | Improving | |
| | | | | | 104 | 11/12/30 | Stationary | |
| 2012 | 15 | F | Com | 5 | 91 | 9/ 5/30 | Stationary | |
| | | | | | 110 | 9/26/30 | Improving | |
| | | | | | 109 | 11/26/30 | Improving | |
| 2159 | 12 | F | Com | 2 | 139 | 9/ 6/30 | Improving | Unregulated diet; no digestive disorders |
| | | | | | 96 | 9/27/30 | Improving | |
| | | | | | 99 | 12/20/30 | Stationary | |
| 2130 | 24 | F | Pu | 5 | 89 | 9/ 6/30 | Aggravated | Indigestion; eats excessive sweets; aggravated by menses |
| | | | | | 93 | 10/ 5/30 | Improving | |
| | | | | | 98 | 11/15/30 | Stationary | |
| 1868 | 18 | F | Com | .. | 97 | 7/25/30 | Good | |
| | | | | | 85 | 8/18/30 | Improving | |
| | | | | | 92 | 9/ 8/30 | Very good | |
| | | | | | 119 | 10/ 5/30 | Same | |
| 1099 | 19 | F | Pu | 5 | 101 | 9/13/30 | Aggravated | Avoids sweets and fried foods |
| | | | Pa | | 103 | 10/11/30 | Stationary | |
| | | | | | 103 | 11/19/30 | New lesions | |
| 2189 | 14 | F | Com | 2 | 110 | 9/15/30 | Improving | Unregulated diet; aggravated by menses |
| | | | | | 102 | 10/ 8/30 | Improving | |
| | | | | | 102 | 11/ 8/30 | Improving | |
| 1946 | 14 | F | Com | 2 | 81 | 7/17/30 | Improving | Unregulated diet |
| | | | | | 88 | 8/ 8/30 | Improving | |
| | | | | | 97 | 10/ 4/30 | Stationary | |
| 1461 | 21 | M | Seb | 3 | 78 | 7/19/30 | Improving | Unregulated diet |
| | | | | | 130 | 8/25/30 | Improving | |
| | | | | | 93 | 9/22/30 | New pustules | |
| 1874 | 20 | F | Pu | 4 | 105 | 7/21/30 | New pustules | |
| | | | | | 82 | 8/20/30 | Improving | |
| | | | | | 107 | 9/27/30 | Aggravated | |

TABLE 1.—*Multiple Blood Sugar Determinations in Fifty-Seven Cases of Acne Vulgaris—Continued*

| Case | Age | Sex | Predominating Type of Lesion* | Duration, Yr. | Blood Sugar, Mg. per 100 Cc. | Date of Determination | Clinical Observations | Diet and Comment |
|---|---|---|---|---|---|---|---|---|
| 1536 | 17 | F | Com | 3 | 110 | 7/21/30 | Improving | Much fatty food and sweets; aggravated by menses |
| | | | | | 90 | 8/20/30 | Improved | |
| | | | | | 99 | 9/13/30 | Stationary | |
| 1784 | 22 | F | Seb | 1 | 98 | 7/21/30 | Improving | Unregulated diet; no constipation; not affected by menses |
| | | | | | 102 | 8/22/30 | Stationary | |
| | | | | | 122 | 10/ 4/30 | Improving | |
| 1969 | 15 | F | Pu | 5 | 73 | 7/23/30 | No improvement | |
| | | | | | 92 | 9/ 5/30 | No improvement | |
| | | | | | 86 | 10/ 5/30 | Improving | |
| 1831 | 38 | F | Pu | 14 | 79 | 7/23/30 | Improving | |
| | | | | | 92 | 8/22/30 | Stationary | |
| | | | | | 94 | 9/17/30 | Improving | |
| 740 | 25 | M | Pa | 8 | 76 | 8/ 1/30 | Stationary | |
| | | | | | 90 | 9/10/30 | Improving | |
| | | | | | 102 | 12/ 6/30 | Improving | |
| 1980 | 21 | F | Pu | 4 | 143 | 8/ 2/30 | Few new pustules | Restricted diet; aggravated by menses |
| | | | | | 102 | 9/ 6/30 | Stationary | |
| | | | | | 93 | 9/27/30 | Improving | |
| 1802 | 20 | F | ..... | 8 | 72 | 7/18/30 | New lesions appearing | Not aggravated by menses |
| | | | | | 97 | 9/13/30 | Improved | |
| 1835 | 25 | F | Com | .. | 94 | 7/19/30 | Stationary | |
| | | | | | 95 | 8/ 9/30 | Improving | |
| 1727 | 17 | M | Pu | 1 | 85 | 7/23/30 | Improving | Unregulated diet; not constipated |
| | | | | | 91 | 8/18/30 | Improving | |
| 2064 | 22 | F | Pa | 3 | 104 | 8/15/30 | Improving | Aggravated by menses |
| | | | | | 102 | 9/20/30 | Improving | |
| 859 | 17 | M | Com | 1 | 78 | 8/20/30 | Stationary | Unregulated diet; overweight |
| | | | | | 108 | 10/25/30 | Improving | |
| 2091 | 13 | F | Com | 1 | 89 | 8/22/30 | Improving | Unregulated diet |
| | | | Pu | | 112 | 9/ 6/30 | Aggravated | |
| 1832 | 18 | F | Com | 3 | 91 | 8/22/30 | Face clear; chest same | |
| | | | Hyp | | 112 | 9/19/30 | Slight improvement | |
| 1722 | 20 | F | Com | 3 | 108 | 9/ 6/30 | Improving | Chronic constipation |
| | | | | | 86 | 9/27/30 | Stationary | |
| 1424 | 25 | F | Com | 5 | 79 | 9/27/30 | Stationary | Unregulated diet; constipated; aggravated by menses |
| | | | | | 98 | 11/15/30 | Improving | |
| 2037 | 25 | F | Com | 5 | 89 | 8/ 8/30 | | |
| | | | | | 103 | 10/ 6/30 | | |

related to clinical changes in the disease. Hence, it would appear that the true representation of the cases showing hyperglycemia lies somewhere between 10 and 20 per cent. Assuming a value of 15 per cent, it would seem most logical to conclude that in cases of acne vulgaris no hyperglycemia exists, as a fair percentage of normal persons are known at times to show a blood sugar slightly in excess of 110 mg. under the conditions of the present investigation.

Table 1 A records the results of single determinations on a group of forty-eight patients with acne. Obviously, no conclusions can be drawn from this group in respect to clinical changes. This group, however,

TABLE 1 A.—*Single Blood Sugar Determinations in Fifty-Six Cases of Acne Vulgaris*

| Case | Blood Sugar, Mg. per 100 Cc. | Case | Blood Sugar, Mg. per 100 Cc. | Case | Blood Sugar, Mg. per 100 Cc. | Case | Blood Sugar, Mg. per 100 Cc. | Case | Blood Sugar, Mg. per 100 Cc. | Case | Blood Sugar, Mg. per 100 Cc. |
|---|---|---|---|---|---|---|---|---|---|---|---|
| 1399 | 88 | 1647 | 94 | 1838 | 98 | 1965 | 89 | 702 | 86 | 312 | 109 |
| 1284 | 80 | 2025 | 77 | 1481 | 96 | 2016 | 93 | 2085 | 91 | 1281 | 103 |
| 1626 | 114 | 1829 | 94 | 2183 | 90 | 2174 | 93 | 1509 | 103 | 2255 | 91 |
| 2264 | 108 | 1378 | 101 | 2287 | 93 | 2256 | 94 | 2038 | 102 | 1796 | 95 |
| 1923 | 80 | 710 | 98 | 1949 | 78 | 1271 | 76 | 1917 | 103 | 1738 | 99 |
| 2114 | 99 | 1309 | 114 | 2193 | 97 | 2127 | 95 | 2144 | 98 | 2138 | 87 |
| 1138 | 86 | 2167 | 89 | 1746 | 96 | 2161 | 90 | 2172 | 85 | 2210 | 159 |
| 227 | 94 | 2209 | 86 | 361 | 99 | 2211 | 82 | 2331 | 85 | 2276 | 110 |

is comparable to investigations as ordinarily reported involving single determinations. In this series of forty-eight cases three determinations, or 6 per cent, were above 110 mg., and three, or 6 per cent, were below 80 mg. This places 88 per cent within the normal range, or 94 per cent if it is assumed that the hypoglycemic cases were probably due to fasting.

### SEBORRHEA, PSORIASIS AND EPIDERMOPHYTOSIS

*Review of the Literature.*—The close association of acne vulgaris with seborrhea prompted the study of the blood sugar level of this disease as well as that of seborrheic dermatitis. The marked contrast in the clinical characteristics of the scales of seborrheic dermatitis and psoriasis prompted the inclusion of the latter disease in this study. Growing interest in blood sugar studies of ringworm fungus infection, especially of the lower extremities, led to the inclusion of this disease in this investigation.

In an extended study of diabetic patients Greenwood [8] observed a higher incidence of infectious and noninfectious skin diseases, although the liability to fungus infection was about the same as in nondiabetic patients. He expressed the belief that it is possible that hyperglycemia may be an etiologic factor in certain skin diseases. In connection with the liability to fungus infection, it is interesting to note that Weidman [9] applied dextrose solution to fungus-negative lesions for one week, after which the lesions were shown in many cases to have become fungus-positive. It is commonly known that the skin and the perspiration contain dextrose in a quantity closely paralleling, but by no means equal to, that of the blood, although no relation has ever been demonstrated between susceptibility to fungus infection and the quantity of dextrose in the skin or perspiration. Van Dyck and his associates [10] concluded

8. Greenwood, A. M.: A Study of the Skin in Five Hundred Cases of Diabetes, J. A. M. A. **89**:774 (Sept. 3) 1927.

9. Weidman, F. D.: Laboratory Aspects of Epidermophytosis, Arch. Dermat. & Syph. **15**:415 (April) 1927.

10. Van Dyck, L. S.; Kingsbury, J.; Throne, B., and Myers, C. N.: The Use of Trichophytin as a Diagnostic and Therapeutic Agent in Mycotic Infections of the Skin, N. Y. State J. Med. **31**:611 (May 15) 1931.

from a study of 100 cases of ringworm that hyperglycemia usually exists in epidermophytosis. By their method of determining blood sugar, the upper normal limit was 100 mg. per hundred cubic centimeters, while the average blood sugar value in their 100 cases was 106 mg.

Reports on the relation of the blood sugar to psoriasis are conflicting. Pels [11] in 1915 reported the blood sugar in seven cases of psoriasis to vary from 95 to 132 mg., with an average of 118 mg. Pick [12] found an almost constant elevation of the blood sugar in his fifteen cases, the average being 135 mg. Throne and Myers [13] reported normal dextrose in thirty-five cases of psoriasis. Schamberg and Brown [4] found the

TABLE 2.—*Blood Sugar in Thirteen Cases of Seborrhea*

| Case | Age | Sex | Duration, Yr. | Blood Sugar, Mg. per 100 Cc. | Dates of Determination | Clinical Observations | Areas Affected | Type of Seborrhea |
|---|---|---|---|---|---|---|---|---|
| 1311 | 22 | F | 5 | 91<br>85<br>93 | 8/ 6/30<br>8/27/30<br>9/26/30 | Stationary<br>Stationary<br>Stationary | Scalp; endocrine dysfunction | Dermatitis |
| 1947 | 30 | F | 10 | 86<br>82 | 7/17/30<br>8/ 8/30 | .....<br>Improved | Entire body surface | Oleosa |
| 254 | 40 | M | 15 | 81<br>95 | 7/15/30<br>11/29/30 | Aggravated<br>Improved | Face, scalp | Dermatitis |
| 1220 | 22 | M | 3 | 82<br>95 | 8/ 6/30<br>8/30/30 | Stationary<br>Stationary | Scalp | Sicca |
| 2055 | 34 | F | 1 | 80 | ..... | ..... | Scalp | Sicca |
| 1560 | 24 | F | 5 | 93 | ..... | ..... | Scalp | Dermatitis |
| 1699 | 23 | F | 10 | 94 | ..... | ..... | Scalp | Sicca |
| 2233 | 20 | M | ½ | 103 | ..... | ..... | Scalp | Sicca |
| 326 | 60 | F | .. | 147 | ..... | ..... | Neck, shoulders, chest, abdomen | Dermatitis |
| 2215 | 38 | M | 2 | 136 | ..... | ..... | Scalp, shoulders, back | Dermatitis |
| 2492 | 20 | M | 2 | 103 | ..... | ..... | Neck, back, knees | Dermatitis |
| 1872 | 30 | F | 2 | 109 | ..... | ..... | Scalp | Dermatitis |
| 2423 | 22 | M | 4 | 98 | ..... | ..... | Face, scalp | Oleosa |

blood sugar in seventy-four cases to vary from 65 to 150 mg., with a few readings above 150 mg. In nine cases, Levin and Kahn found the blood sugar above 110 mg. in only one (i. e., 220 mg.).

*Comment.*—Table 2 records the results of eighteen blood sugar determinations in thirteen cases of seborrheic dermatitis. In one case three and in three cases two determinations were made on each patient, which are too few to substantiate any conclusions regarding the relation

11. Pels, I. R.: The Sugar Content of the Blood in Certain Diseases of the Skin, J. A. M. A. **65**:2077 (Dec. 11) 1915.

12. Pick, W.: Blood Sugar Estimation in Psoriasis, Furunculosis, and Syphilis, Dermat. Wchnschr. **72**:297, 1918.

13. Throne, B., and Myers, C. N.: Psoriasis: Blood Chemistry Studies; Treatment, New York State J. Med. **28**:914, 1928.

of the blood sugar to the clinical changes. Of the eighteen determinations, only two, or 11 per cent, were above 110 mg. Based on the number of persons rather than on the number of determinations, in two

TABLE 3.—*Blood Sugar in Nine Cases of Psoriasis*

| Case | Age | Sex | Duration, Yr. | Blood Sugar, Mg. per 100 Cc. | Dates of Determination | Clinical Observations | Areas Affected | Comment |
|---|---|---|---|---|---|---|---|---|
| 1300 | 37 | M | 11 | 94<br>93 | 7/23<br>10/ 8 | Stationary<br>Stationary | Entire body surface, face, scalp | |
| 2380 | 45 | F | 25 | 98 | 10/18 | Stationary | Arms, trunk, knees | Same summer and winter |
| 1896 | 48 | M | 1 | 83 | ..... | ..... | Scalp; 1 patch below knee, 1 on ankle | |
| 2001 | 33 | M | .. | 90 | ..... | ..... | Legs, elbow | Intermittent |
| 2224 | 40 | M | 15 | 98 | ..... | ..... | Scalp, shoulder, arms | |
| 1569 | 42 | F | 17 | 102 | ..... | ..... | Arms, forehead | Made worse in winter and by "nervousness" |
| 2496 | 47 | M | 1/10 | 97 | ..... | ..... | Forehead, arms, legs | Lesions increasing first visit |
| 867 | 26 | F | 5 | 103 | ..... | ..... | Old lesions clearing, new appearing on arms chest, abdomen | |
| 591 | 38 | F | 3 | 94 | ..... | ..... | Arms, trunk, legs | Aggravated by "nervousness" |

TABLE 4.—*Blood Sugar in Thirteen Cases of Vegetable Parasitic Infection*

| Case | Age | Sex | Duration, Years | Blood Sugar, Mg. per 100 Cc. | Dates of Determination | Clinical Observations | Type of Infection |
|---|---|---|---|---|---|---|---|
| 2065 | 17 | F | 7 | 98<br>106 | 11/ 8/30<br>12/ 3/30 | Improving<br>Improving | Tinea favosa |
| 2306 | 23 | F | 1 | 98<br>100 | 11/12/30<br>12/ 6/30 | Improving<br>Stationary | Trichophytid |
| 2421 | 18 | M | .. | 98 | ..... | ..... | Tinea cruris |
| 2316 | 30 | F | 6 | 97 | ..... | ..... | Eczematoid ringworm |
| 2486 | 58 | F | 4 | 94 | ..... | ..... | Eczematoid ringworm |
| 2477 | 45 | F | .. | 99 | ..... | ..... | Eczematoid ringworm |
| 2464 | 49 | M | 1/10 | 101 | ..... | ..... | Eczematoid ringworm |
| 2376 | 37 | F | 2 | 103 | ..... | ..... | Eczematoid ringworm |
| 2328 | 29 | F | ½ | 105 | ..... | ..... | Trichophytid |
| 5255 | 26 | F | 7 | 99 | ..... | ..... | Eczematoid ringworm |
| 1050 | 35 | M | .. | 106 | ..... | ..... | Eczematoid ringworm |
| 2595 | 30 | M | 3 | 95 | ..... | ..... | Eczematoid ringworm |
| 2521 | 40 | M | 1 | 95 | ..... | ..... | Eczematoid ringworm |

instances of the thirteen, or about 15 per cent, the blood sugar was above 110 mg.

Table 3 records the results of ten blood sugar determinations in nine cases of psoriasis of varying degrees of severity. Of the ten determinations, none is outside the normal limits. It is therefore appar-

ent that from these statistics there is no relation between the blood sugar and the extent of the disease, either considered alone or in connection with age, sex or duration.

Table 4 records the results of fifteen blood sugar determinations on thirteen patients with several types of vegetable parasitic infection. Of the fifteen determinations, all are within normal limits. Although the number of cases is too few to substantiate a definite conclusion, there appears to be no relation between the blood sugar and the type of infection.

## CONCLUSIONS

1. The results of the present investigation, as regards acne vulgaris, substantiate the preliminary findings and conclusions of Strickler and Saylor.

2. Of 202 blood sugar determinations in 101 cases of acne vulgaris, 10 per cent were above 110 mg. per hundred cubic centimeters. Of 101 patients, 19 per cent at some time during the period of observation showed a blood sugar value above 110 mg. Of the group of single determinations covering 48 of the cases of acne vulgaris, 88 per cent fell within from 80 to 110 mg. Assuming 15 per cent to be a true representation of cases exhibiting hyperglycemia, it is concluded that acne vulgaris is not characterized by hyperglycemia, as a fair percentage of normal persons at times may be slightly hyperglycemic.

3. Changes in the blood sugar in individual cases over periods of as long as three months do not coincide with clinical improvement or relapse.

4. No particular type of acne vulgaris is characterized by either hypoglycemia or hyperglycemia, nor are the two factors, blood sugar and clinical change, related to sex, age or duration of the disease.

5. Hyperglycemia probably is not associated with seborrhea (11 per cent of eighteen determinations in thirteen cases were above 110 mg.), psoriasis (ten determinations in nine cases were all normal) or vegetable parasitic infections (fifteen determinations in thirteen cases were all normal). Although the number of cases in these latter diseases is small, it indicates that in a larger number of cases hyperglycemia probably would not prove characteristic.

6. In respect to all the diseases reported, the observation may be correct that a diet rich in sugar or other carbohydrates is inimical, particularly for certain patients with acne vulgaris, but this claim is not substantiated by the actual changes in the blood sugar. It is possible that excessive carbohydrates exert an indirect effect on this disease which is not demonstrable by the present type of chemical studies of the blood.

# CHOLESTEROL METABOLISM IN CERTAIN DERMATOSES

## WITH SPECIAL REFERENCE TO ACNE VULGARIS

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Numerous studies in recent years have attempted to relate various skin diseases to changes in the composition of the blood. The results of such studies have been largely disappointing, showing either the constituents determined to be normal or the variations so irregular as to make deductions therefrom impossible.

The high content of cholesterol and its esters as well as of other sterols in the normal skin secretion makes its variations an interesting subject as a possible predisposing factor in certain dermatoses. The fact that cholesterol plays a prominent part in lymphoid defense, its ability to protect blood cells from hemolysis and the universal presence of cholesterol or related sterols in plant and animal cells might lead one to suspect cholesterol of a prominent part in the etiology or course of such inflammatory diseases as acne and psoriasis, or the seborrheic dermatoses in which the skin may secrete either excessive or subnormal quantities of sebum (which normally contains appreciable quantities of cholesterol).

The present study of the cholesterol content of the blood was undertaken to determine: (1) whether there is any relation between the cholesterol content of the blood and certain skin diseases, and (2) whether there is any variation during the course of the disease, particularly in the diseases that are characterized by periods of remission, such as acne and psoriasis.

### PLAN OF INVESTIGATION

Cholesterol in the whole blood and dextrose were determined from the same sample. Hence, the plan of this investigation follows that of a preceding paper.[1] Cholesterol was determined in whole blood by the

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1. Strickler, A., and Adams, P. D.: Blood Sugar Metabolism in Certain Dermatoses: With Special Reference to Acne Vulgaris, Arch. Dermat. & Syph., this issue, p. 1.

method of Myers and Wardell.[2] The normal range of cholesterol was taken as from 130 to 170 mg. per hundred cubic centimeters of whole blood.

## REVIEW OF THE LITERATURE

The general literature on the cholesterol content of the blood presents results of wide variability. Normal values of cholesterol as reported in the literature may be as low as 110 mg. or as high as 250 mg. per hundred cubic centimeters of whole blood, although various textbooks of physiologic chemistry (e. g., Hawk and Bergeim and Mathews) state that the normal limits of cholesterol in whole blood are from 130 to 170 mg. In an extended study of "normal" men and clinical patients, Petersen and Levinson[3] placed normal cholesterol at from 160 to 245 mg. In a comparative study of the simultaneous variations of dextrose and cholesterol in diabetic patients, McCrudden and Sargent[4] stated that in diabetes the two are not related, and they reported normal values as high as 209 mg. Rosen and Krasnow,[5] in a statistical study of the results of cholesterol determinations on thirty normal medical students, found values as low as 111, 119 and 126 mg., and as high as 193 mg. Gorham and Myers[6] placed normal variations on an uncontrolled diet at from 130 to 190 mg. per hundred cubic centimeters of whole blood. Bloor[7] stated that the average value for men is 210 mg., and for women, 230 mg. Numerous contradictory reports of normal subjects in the literature might find partial explanation in the excellent critical study of Luden.[8]

In spite of its great importance as one of the cell lipoids, the function of cholesterol and related sterols in animal metabolism is far from known. Burger and Schlomka[9] stated that the cholesterol content of

2. Myers and Wardell, in Hawk and Bergeim: Practical Physiological Chemistry, ed. 9, Philadelphia, P. Blakiston's Son & Company, 1927, p. 391.

3. Petersen, W. F., and Levinson, S. A.: The Skin Reactions, Blood Chemistry and Physical Status of Normal Men and of Clinical Patients, Arch. Path. **9**:151 (Jan.) 1930.

4. McCrudden, F. H., and Sargent, C. S.: Comparison of the Glucose and Cholesterol Content of the Blood, J. Biol. Chem. **33**:387, 1918.

5. Rosen, I., and Krasnow, F.: Cholesterol Studies in Syphilis, Arch. Dermat. & Syph. **20**:75 (July) 1929.

6. Gorham, F. D., and Myers, V. C.: Remarks on the Cholesterol Content of Human Blood, Arch. Int. Med. **20**:599 (Oct.) 1917.

7. Bloor, W. R.: J. Biol. Chem. **25**:577, 1916.

8. Luden, Georgine: Studies on Cholesterol: VI. The Value of Blood Cholesterol Determinations and Their Place in Cancer Research, J. Lab. & Clin. Med. **4**:719, 1918.

9. Burger, M., and Schlomka, G.: Aging of Tissue, Ztschr. f. d. ges. exper. Med. **63**:105, 1928.

the skin decreases with increasing age. Roffo [10] found that the percentage of cholesterol in the dry matter of the skin of the face is greater than that in the dry matter of the skin of the abdomen, although the percentage of cholesterol in the subcutaneous fat of the two regions is practically the same. He stated further that the skin of males contains a greater percentage of cholesterol than the skin of females. Small [11] stated that there is a decrease in blood cholesterol in old age. Pachur [12] found that the fat content of the skin increases in puberty and decreases in old age. The secretion of sebum is increased in a majority of cases of eczema and acne vulgaris. Rosen and Krasnow [13] examined the blood of eighty patients with dermatophytosis and found the values for cholesterol to be fairly evenly distributed between 130 and 180 mg. per hundred cubic centimeters, and in eleven cases of psoriasis the values varied from 135 to 196 mg. Fischl [14] reported that the cholesterol content of the blood tends to be high in the dermatoses that are not accompanied by fever. Levin and Kahn [15] examined the blood cholesterol in cases of xanthoma and found it above normal (210 mg.). Rosen and Krasnow [5] stated that in syphilis the cholesterol content of the blood is low in the initial stages of the disease, but tends to increase, approaching normal as the disease advances from primary to tertiary stages. Gorham and Myers [6] examined fifteen cases of syphilis and found the blood cholesterol to vary from 120 to 190 mg., which is within the limits they found to be normal.

That cholesterol has considerable influence on phagocytosis and plays some part in immunity to certain diseases has been known for many years, although the exact function of the cholesterol is unknown. Dewey and Nuzum [16] observed that injections of a colloidal suspension of cholesterol into guinea-pigs has a depressing effect on phagocytosis and delays antibody formation. Luden [17] stated that a diet that increases

10. Roffo, A. H.: The Cholesterol Content of the Skin, Néoplasmes **7**:344, 1928.

11. Small, J. C.: Role of Cholesterol in Pathology, J. Lab. & Clin. Med. **1**:809, 1915.

12. Pachur, Reinhold: The Secretion of Sebum on the Human Skin Surface, Arch. f. Dermat. u. Syph. **162**:253, 1930.

13. Rosen, I., and Krasnow, F.: Lecithin and Cholesterol Studies in Dermatophytosis, Arch. Dermat. & Syph. **23**:132 (Jan.) 1931.

14. Fischl, F.: Wien. klin. Wchnschr. **27**:982, 1914.

15. Levin, O. L., and Kahn, Max: The Chemistry of the Body in Diseases of the Skin, Am. J. M. Sc. **162**:698, 1921.

16. Dewey, K., and Nuzum, F.: The Effect of Cholesterol on Phagocytosis, J. Infect. Dis. **15**:472, 1914.

17. Luden, Georgine: Studies on Cholesterol: IV. Experiments Concerning the Relation of the Diet, the Blood Cholesterol, and the "Lymphoid Defense," J. Lab. & Clin. Med. **3**:141, 1917.

blood cholesterol weakens the lymphoid defense, and one that decreases blood cholesterol stimulates it. Borchardt,[18] however, fed cholesterol to cats and found that it increased the ability of these animals to overcome artificial staphylococcus infection. In a recent publication, Plaut and Kassowitz[19] stated that cholesterol makes organ extracts more reactive with certain antiserums, not because of any antigenic properties of the cholesterol, but because of some physicochemical action. Dewey and Nuzum[16] injected cholesterol into guinea-pigs and rabbits and found that phagocytosis was lowered by direct action on the phagocytes.

## COMMENT

In tables 1 and 1 A are the results of 217 determinations in 103 cases of acne vulgaris.

In considering the cases involving three and four determinations on each patient, it will be seen that there is no regular variation in cholesterol as was seen in dextrose. An examination of the clinical changes in the cases in which two, three and four determinations were made shows that there is no relation between the changes in blood cholesterol and either improvement or relapse. There is also no relation between the cholesterol content and the type of lesion.

Of the 217 determinations, two, or 1 per cent, fall between 120 and 130 mg.; 164 or 75 per cent, fall between 131 and 170 mg.; twenty-five, or 12 per cent, fall between 171 and 180 mg.; nine, or 4 per cent, fall between 181 and 190 mg.; five, or 2 per cent, fall between 191 and 200 mg., and twelve, or 6 per cent, fall above 201 mg.

Basing the percentage on the number of patients rather than on the number of determinations, it will be seen that at some time during the period of observation of the 113 patients, forty-three, or 38 per cent, had cholesterol above 171 mg.; two, or 2 per cent, had values below 130 mg., while sixty-eight, or 60 per cent, had normal values throughout. If only the first determination throughout is considered, including the single determination in table 1 A, the following distribution is obtained: none below 130 mg.; seventy-seven, or 68 per cent, from 131 to 170 mg.; fourteen, or 12.4 per cent, from 171 to 180 mg.; seven, or 6 per cent, from 181 to 190 mg.; four, or 3.5 per cent, from 191 to 200 mg., and eleven, or 10 per cent, above 200 mg.

With the percentage of cases at some time showing hypercholesteremia as a minimum value, it can be concluded that not less than about

18. Borchardt, W.: The Significance of Cholesterol in Experimental Staphylococcus Infection in Cats, Klin. Wchnschr. **8**:1179, 1929.

19. Plaut, F., and Kassowitz, H.: Cholesterol as Antigen, Ztschr. f. Immunitätsforsch. u. exper. Therap. **66**:152, 1930.

TABLE 1.—*Multiple Blood Cholesterol Determinations in Fifty-Seven Cases of Acne Vulgaris*

| Case | Age | Sex | Type of Lesion* | Duration, Yr. | Cholesterol, Mg. | Dates of Determination | Clinical Observations | Diet and Other Factors |
|---|---|---|---|---|---|---|---|---|
| 1398 | 20 | F | Pa | 3 | 172 | 8/ 8/30 | Very few papules..... | Vegetable |
| | | | | | 161 | 9/ 5/30 | Improving | |
| | | | | | 176 | 10/ 1/30 | Generally improving | |
| | | | | | 154 | 10/18/30 | Stationary | |
| 563 | 16 | M | Seb | 1 | 158 | 7/15/30 | ..... | Much potatoes; no sweets or fried foods |
| | | | | | 153 | 8/22/30 | Improving | |
| | | | | | 132 | 10/11/30 | Improving | |
| | | | | | 133 | 10/25/30 | Stationary | |
| 1709 | 24 | M | Pa | 6 | 221 | 7/19/30 | Numerous inflamed papules. | Good health |
| | | | | | 163 | 8/18/30 | Slight improvement | |
| | | | | | 176 | 9/10/30 | Stationary | |
| | | | | | 164 | 10/10/30 | Slight improvement | |
| 1641 | 34 | F | Seb | 20 | 206 | 7/19/30 | Numerous lesions and pustules | No change during menses |
| | | | | | 155 | 9/ 8/30 | Improved—stationary | |
| | | | | | 139 | 10/ 8/30 | Same | |
| | | | | | 144 | 10/18/30 | Improving | |
| 1841 | 20 | M | Pu | .. | 191 | 7/19/30 | Improving..... | Careful of diet; constipation and indigestion |
| | | | | | 174 | 8/13/30 | Improving | |
| | | | | | 172 | 9/10/30 | Few new pustules | |
| | | | | | 143 | 10/ 3/30 | Condition fair | |
| 1971 | 30 | M | Pu | .. | 173 | 7/23/30 | Stationary | |
| | | | | | 171 | 8/18/30 | New lesions; worse | |
| | | | | | 210 | 9/ 8/30 | Slightly improved | |
| | | | | | 170 | 10/ 3/30 | Same | |
| 1968 | 19 | M | Pu | .. | 134 | 7/23/30 | Numerous scars and pustules | Careless about diet; no constipation |
| | | | | | 158 | 8/ 2/30 | Improving | |
| | | | | | 136 | 9/19/30 | Condition stationary | |
| | | | | | 158 | 10/18/30 | Improving | |
| 1347 | 20 | M | Pu | .. | 170 | 7/25/30 | Slight improvement; stationary | Good health; no constipation |
| | | | | | 148 | 8/18/30 | Improving | |
| | | | | | 142 | 9/ 8/30 | Very much better | |
| | | | | | 164 | 10/ 1/30 | Stationary | |
| 1868 | 18 | F | Com | .. | 165 | 7/25/30 | Good | |
| | | | | | 145 | 8/18/30 | Improving | |
| | | | | | 159 | 9/ 8/30 | Very good | |
| | | | | | 148 | 10/ 5/30 | Same | |
| 1099 | 19 | F | Pa Pu | 5 | 213 | 9/13/30 | Becoming worse..... | Avoids sweets and fried foods |
| | | | | | 169 | 10/11/30 | Stationary..... | |
| | | | | | 183 | 11/19/30 | New lesions | |
| 2189 | 14 | F | Com | 2 | 154 | 9/15/30 | Improving..... | Irregular diet; worse during menses |
| | | | | | 139 | 10/ 8/30 | Improving | |
| | | | | | 135 | 11/ 8/30 | Improving | |
| 2219 | 15 | M | Pu | 3 | 152 | 9/19/30 | Improving..... | Careful of diet; no constipation |
| | | | | | 150 | 10/ 8/30 | Improving; few new lesions | |
| | | | | | 154 | 11/12/30 | Same | |
| 2220 | 17 | M | Pu | 2 | 135 | 9/19/30 | Stationary..... | Constipation; unregulated diet |
| | | | | | 153 | 11/ 8/30 | Improving | |
| | | | | | 145 | 12/ 6/30 | Stationary | |
| 2045 | 21 | F | Pu | 6 | 139 | 8/ 9/30 | Improving..... | Constipated; not careful of diet; worse during menses |
| | | | | | 143 | 9/13/30 | Better | |
| | | | | | 139 | 10/11/30 | Much improved | |
| 1059 | 17 | F | Pu | 2 | 148 | 8/13/30 | Slowly improving..... | Blood sugar, 115 mg.; eats abundantly of fats and sweets; worse during menses |
| | | | | | 147 | 9/12/30 | Slowly improving | |
| | | | | | 158 | 10/11/30 | Stationary | |
| 1901 | 16 | M | Pu | 3 | 142 | 8/13/30 | Many new pustules..... | Unregulated diet |
| | | | | | 153 | 9/15/30 | Stationary | |
| | | | | | 177 | 10/10/30 | Aggravated | |
| 1994 | 20 | M | Pu | 2 | 162 | 8/23/30 | New pustules forming | |
| | | | | | 149 | 9/27/30 | Improving | |
| | | | | | 145 | 10/25/30 | Slowly improving | |

TABLE 1.—*Multiple Blood Cholesterol Determinations in Fifty-Seven Cases of Acne Vulgaris—Continued*

| Case | Age | Sex | Type of Lesion* | Duration, Yr. | Cholesterol, Mg. | Dates of Determination | Clinical Observations | Diet and Other Factors |
|---|---|---|---|---|---|---|---|---|
| 1414 | 19 | M | Pa | 2 | 150<br>142<br>165 | 8/25/30<br>9/20/30<br>11/26/30 | Steadily improving.....<br>Same<br>Stationary | Unregulated diet |
| 944 | 18 | M | Pa<br>Com | 3 | 154<br>163<br>165 | 8/27/30<br>9/17/30<br>11/12/30 | New lesions appearing<br>Slightly improved<br>Same | |
| 2012 | 15 | F | Com | ½ | 133<br>135<br>131 | 9/ 5/30<br>9/26/30<br>11/26/30 | Stationary<br>Slight improvement<br>Slight improvement | |
| 21 | 18 | F | Pu | 3 | 146<br>160 | 8/15/30<br>10/ 1/30 | New pustules appearing<br>Slowly improving | |
| 1708 | 18 | F | Hyp | 3 | 172<br>141 | 9/ 6/30<br>10/ 5/30 | Stationary<br>Same | |
| 1802 | 20 | F | .... | 8 | 182<br>144 | 7/18/30<br>9/13/30 | New lesions appearing.....<br>Much improved | Not aggravated by menses |
| 1835 | 25 | F | Com | .. | 233<br>131 | 7/19/30<br>8/ 9/30 | Improving | |
| 1727 | 17 | M | Pu | 1 | 214<br>145 | 7/23/30<br>8/18/30 | Improving.....<br>Improving | Not constipated; diet unregulated |
| 2064 | 22 | F | Pa | 3 | 146<br>137 | 8/15/30<br>9/20/30 | Improving.....<br>Improving | Aggravated by menses |
| 1120 | 24 | F | Pa | 8 | 163<br>180 | 8/16/30<br>9/13/30 | Improving.....<br>Improving | Diet unregulated |
| 859 | 17 | M | Com | 1 | 147<br>169 | 8/20/30<br>10/25/30 | Stationary.....<br>Improving | Heavy eater; overweight; unregulated diet |
| 2091 | 13 | F | Com<br>Pu | 1 | 154<br>180 | 8/22/30<br>9/ 6/30 | Improving.....<br>New pustules | Unregulated diet |
| 1832 | 18 | F | Com<br>Hyp | 3 | 167<br>145 | 8/22/30<br>9/19/30 | Face clear; chest same<br>Slight improvement | |
| 1722 | 20 | F | Com | 3 | 138<br>125 | 9/ 6/30<br>9/27/30 | Slight improvement.....<br>Stationary | Constipated |
| 1424 | 25 | F | Com | 5 | 174<br>198 | 9/27/30<br>11/15/30 | No improvement.....<br>Slight improvement | Aggravated by menses; constipated; unregulated diet |
| 2037 | 25 | F | Com | 5 | 140<br>146 | 8/ 8/30<br>10/ 6/30 | | |
| 2209 | 26 | F | Pu | 1/12 | 130<br>153 | 9/17/30<br>2/ 7/30 | Stationary<br>Stationary | |
| 2159 | 12 | F | Com | 2 | 154<br>152<br>178 | 9/ 6/30<br>9/27/30<br>12/20/30 | Improving.....<br>Improving<br>No improvement | No indigestion; unregulated diet |
| 2130 | 24 | F | Pu | 5 | 137<br>153<br>165 | 9/ 6/30<br>10/ 5/30<br>11/15/30 | New lesions appearing.....<br>Slight improvement<br>Same | Worse during menses; indigestion; excessive sweets |
| 1946 | 14 | F | Com | 2 | 154<br>143<br>149 | 7/17/30<br>8/ 8/30<br>10/ 4/30 | Improving.....<br>Improving<br>Stationary | Unregulated diet |
| 1461 | 21 | M | Seb | 3 | 244<br>165<br>169 | 7/19/30<br>8/25/30<br>9/22/30 | Slowly improving.....<br>Slowly improving<br>New pustules | Unregulated diet |
| 1874 | 20 | F | Pu | 4 | 184<br>153<br>145 | 7/21/30<br>8/20/30<br>9/27/30 | New pustules<br>Slight improvement<br>Worse | |
| 1536 | 17 | F | Com | 3 | 248<br>145<br>172 | 7/21/30<br>8/20/30<br>9/13/30 | Generally improving.....<br>Much improved<br>Same | Worse during menses; much fats and sweets |

TABLE 1.—*Multiple Blood Cholesterol Determinations in Fifty-Seven Cases of Acne Vulgaris—Continued*

| Case | Age | Sex | Type of Lesion* | Duration, Yr. | Cholesterol, Mg. | Dates of Determination | Clinical Observations | Diet and Other Factors |
|---|---|---|---|---|---|---|---|---|
| 1784 | 22 | F | Seb | 1 | 173 | 7/21/30 | Slowly improving | No change during menses; not constipated; unregulated diet |
| | | | | | 138 | 8/22/30 | Stationary | |
| | | | | | 149 | 10/ 4/30 | Slight improvement | |
| 1969 | 15 | F | Pu | 5 | 165 | 7/23/30 | No improvement | |
| | | | | | 171 | 9/ 5/30 | No improvement | |
| | | | | | 142 | 10/ 5/30 | Slight improvement | |
| 1831 | 28 | F | Pu | 14 | 163 | 7/23/30 | Slowly improving | |
| | | | | | 150 | 8/22/30 | Same | |
| | | | | | 143 | 9/17/30 | Improving | |
| 1100 | 17 | F | Seb | 3 | 167 | 7/25/30 | Slight improvement | |
| | | | | | 165 | 9/12/30 | New lesions appearing | |
| | | | | | 197 | 10/ 8/30 | Improving | |
| 740 | 25 | M | Pa | 3 | 136 | 8/ 1/30 | | |
| | | | | | 153 | 9/10/30 | Improving | |
| | | | | | 149 | 12/ 6/30 | Improving | |
| 1730 | 21 | F | Seb | 16 | 191 | 8/ 2/30 | Improved | Regulated diet; chronic constipation |
| | | | | | 166 | 8/25/30 | Stationary | |
| | | | | | 156 | 10/ 4/30 | Stationary | |
| 1980 | 21 | F | Pu | 4 | 206 | 8/ 2/30 | Few new lesions appearing | Aggravated at menses; careful of diet |
| | | | | | 143 | 9/ 6/30 | Stationary | |
| | | | | | 136 | 9/27/30 | Slight improvement | |
| 414 | 22 | F | Pa | 1 | 141 | 8/ 6/30 | Improving | |
| | | | | | 153 | 8/27/30 | No active lesions; improving | |
| | | | | | 146 | 9/17/30 | Same | |
| 141 | 35 | F | Pa | 21 | 149 | 8/16/30 | Improving | Aggravated during menses |
| | | | | | 157 | 10/ 1/30 | Very good | |
| | | | | | 165 | 11/15/30 | Same | |
| 1437 | 21 | F | Seb | ¾ | 132 | 8/22/30 | Improving | |
| | | | | | 129 | 9/12/30 | Slight improvement | |
| | | | | | 149 | 10/18/30 | Stationary | |
| 2156 | 22 | F | Pu | 4 | 131 | 9/ 6/30 | Improving | Aggravated at menses; careful of diet |
| | | | | | 139 | 10/ 1/30 | New lesions | |
| | | | | | 156 | 11/15/30 | Improving | |
| 2179 | 21 | F | Pu | 2 | 193 | 9/12/30 | Stationary | Constipated; unregulated diet |
| | | | | | 148 | 10/ 8/30 | Slight improvement | |
| | | | | | 137 | 11/15/30 | Improved | |
| 2276 | 18 | M | Seb | 2 | 165 | 10/ 4/30 | Stationary | Unregulated diet |
| | | | | | 188 | 2/ 7/31 | Improving | |
| 2040 | 23 | F | Com | 2 | 139 | 8/ 8/30 | Stationary | Not aggravated at menses; unregulated diet |
| | | | | | 132 | 9/ 3/30 | Slight improvement | |
| 999 | 19 | M | Seb | 3 | 147 | 8/11/30 | Improving | Constipated; avoids sweets |
| | | | | | 156 | 9/ 5/30 | No improvement | |
| 1962 | 19 | M | Seb | 3 | 146 | 8/13/30 | Not improving | |
| | | | | | 142 | 10/ 1/30 | Same | |
| 1380 | 17 | M | Pa | 3 | 178 | 8/13/30 | Improving | |
| | | | | | 152 | 9/12/30 | Improving | |

* In this column, Pu indicates pustular; Pa, papular; Com, comedones; Seb, sebaceous, and Hyp, hyperphysiologic.

60 per cent of cases of acne have normal values for cholesterol. Hence it cannot be concluded that acne is definitely characterized by either hypercholesteremia or hypocholesteremia, nor that cholesterol, per se, is definitely involved as an etiologic factor.

TABLE 1 A.—*Single Blood Cholesterol Determinations in Fifty-Six Cases of Acne Vulgaris*

| Case | Blood Cholesterol, Mg. per 100 Cc. | Case | Blood Cholesterol, Mg. per 100 Cc. | Case | Blood Cholesterol, Mg. per 100 Cc. | Case | Blood Cholesterol, Mg. per 100 Cc. | Case | Blood Cholesterol, Mg. per 100 Cc. | Case | Blood Cholesterol, Mg. per 100 Cc. | Case | Blood Cholesterol, Mg. per 100 Cc. |
|---|---|---|---|---|---|---|---|---|---|---|---|---|---|
| 1138 | 151 | 2167 | 137 | 1746 | 140 | 2161 | 155 | 2172 | 153 | 2210 | 154 | 227 | 143 |
| 361 | 185 | 2211 | 136 | 2331 | 162 | 2818 | 190 | 2554 | 173 | 2796 | 155 | 2674 | 150 |
| 2724 | 175 | 2742 | 171 | 2847 | 156 | 2835 | 196 | 241 | 204 | 2646 | 176 | 2038 | 138 |
| 1796 | 157 | 1923 | 160 | 2863 | 169 | 2113 | 178 | 2114 | 142 | 1309 | 145 | 1251 | 140 |
| 2255 | 131 | 2193 | 149 | 2138 | 131 | 710 | 147 | 1949 | 163 | 1271 | 182 | 1917 | 288 |
| 1738 | 154 | 1399 | 177 | 1838 | 140 | 1965 | 211 | 702 | 169 | 312 | 138 | 1284 | 171 |
| 2025 | 146 | 1481 | 145 | 2016 | 148 | 2085 | 134 | 1626 | 134 | 1829 | 182 | 2183 | 163 |
| 2174 | 154 | 1509 | 148 | 2264 | 148 | 1378 | 160 | 2287 | 150 | 2256 | 144 | 2724 | 175 |

TABLE 2.—*Blood Cholesterol in Seventeen Cases of Seborrhea*

| Case | Sex | Age | Duration, Years | Cholesterol, Mg. per 100 Cc. | Dates of Determination | Clinical Observations | Areas Affected | Type of Seborrhea |
|---|---|---|---|---|---|---|---|---|
| 1947 | F | 30 | 10 | 178 | 7/17 | ..... | Entire body surface | Oleosa |
| | | | | 193 | 8/ 8 | Improved | | |
| | | | | 173 | 1/28 | Stationary | | |
| 1311 | F | 22 | 5 | 145 | 8/ 6 | Stationary | Scalp; endocrine dysfunction | Dermatitis |
| | | | | 142 | 8/27 | Stationary | | |
| | | | | 152 | 9/26 | Stationary | | |
| 2423 | M | 22 | 4 | 148 | 11/29 | Improved | Face, scalp | Oleosa |
| | | | | 136 | 2/ 7 | Stationary | | |
| 254 | M | 40 | 15 | 155 | 7/15 | Aggravated | Face, scalp | Dermatitis |
| | | | | 141 | 11/29 | Improved | | |
| 2055 | F | 34 | 1 | 131 | ..... | ..... | Scalp | Sicca |
| 1560 | F | 24 | 5 | 156 | ..... | ..... | Scalp | Dermatitis |
| 1699 | F | 23 | 10 | 149 | ..... | ..... | Scalp | Sicca |
| 1220 | M | 22 | 3 | 153 | ..... | ..... | Scalp | Sicca |
| 2233 | M | 20 | ½ | 158 | ..... | ..... | Scalp | Sicca |
| 326 | F | 60 | .. | 126 | ..... | ..... | Neck, shoulders, chest, abdomen | Dermatitis |
| 2215 | M | 38 | 2 | 174 | ..... | ..... | Scalp, shoulders, back | Dermatitis |
| 2492 | M | 20 | 2 | 153 | ..... | ..... | Neck, back, knees | Dermatitis |
| 1872 | F | 30 | 2 | 171 | ..... | ..... | Scalp | Dermatitis |
| 1412 | F | 48 | 12 | 170 | ..... | ..... | Face, neck, arms, chest, thighs | Dermatitis |
| 1199 | F | 23 | 12 | 185 | ..... | ..... | Scalp, abdomen | Sicca |
| 1546 | F | 32 | 1 | 181 | ..... | ..... | Scalp | Sicca |
| 1815 | F | 30 | 2/10 | 134 | ..... | ..... | Scalp, face, neck, chest | Dermatitis |

Table 2 records the results of twenty-three cholesterol determinations on the whole blood in seventeen cases of seborrhea. It is well known that the skin normally secretes cholesterol. It might be supposed, therefore, that in diseases characterized by excessive "oiliness" or by abnormal dryness the blood would be either high or low in cholesterol.

Of the twenty-three determinations, seven, or 31 per cent, are above 171 mg. (maximum, 193 mg.); one, or 4 per cent, are below 130 mg., and fifteen, or 65 per cent, are normal.

Table 3 records the results of eleven determinations in nine cases of psoriasis. Of the eleven determinations, four, or 36 per cent, are above

TABLE 3.—*Blood Cholesterol in Nine Cases of Psoriasis*

| Case | Age | Sex | Duration, Years | Cholesterol, Mg. per 100 Cc. | Dates of Determination | Clinical Observations | Areas Affected | Comment |
|---|---|---|---|---|---|---|---|---|
| 1300 | 37 | M | 11 | 174<br>197 | 7/23<br>10/ 8 | Stationary<br>Stationary | Entire body surface, face, scalp | |
| 2380 | 45 | F | 25 | 131<br>167 | 10/18<br>11/29 | Stationary<br>Improving | Arms, trunk, knees | Same summer and winter |
| 1896 | 48 | M | 1 | 161 | ..... | ..... | Scalp; 1 patch below knee, 1 on ankle | |
| 2001 | 33 | M | .. | 179 | ..... | ..... | Legs, elbow | Intermittent |
| 2224 | 40 | M | 15 | 149 | ..... | ..... | Scalp, shoulder, arms | |
| 1569 | 42 | F | 17 | 131 | ..... | ..... | Arms, forehead | Worse in winter and aggravated by "nervousness" |
| 2496 | 47 | M | 1/10 | 147 | ..... | ..... | Forehead, arms, legs | Lesions increasing first visit |
| 867 | 26 | F | 5 | 184 | ..... | Old lesions clearing, new appearing | Forehead, arms, chest, abdomen, legs | |
| 591 | 38 | F | 3 | 186 | ..... | ..... | Arms, trunk, legs | Aggravated by "nervousness" |

TABLE 4.—*Blood Cholesterol in Thirteen Cases of Vegetable Parasitic Infection*

| Case | Age | Sex | Duration, Years | Cholesterol, Mg. per 100 Cc. | Dates of Determination | Clinical Observations | Type of Infection |
|---|---|---|---|---|---|---|---|
| 2065 | 17 | F | 7 | 155<br>130 | 11/ 8<br>12/ 3 | Improving<br>Improving | Tinea favosa |
| 2306 | 23 | F | 1 | 130<br>146 | 11/12<br>12/ 6 | Improving<br>Stationary | Trichophytid |
| 2421 | 18 | M | .. | 165 | ..... | ..... | Tinae cruris |
| 2316 | 30 | F | 6 | 169 | ..... | ..... | Eczematoid ringworm |
| 2486 | 58 | F | 4 | 153 | ..... | ..... | Eczematoid ringworm |
| 2477 | 45 | F | .. | 161 | ..... | ..... | Eczematoid ringworm |
| 2464 | 49 | M | 1/10 | 133 | ..... | ..... | Eczematoid ringworm |
| 2376 | 37 | F | 2 | 137 | ..... | ..... | Eczematoid ringworm |
| 2328 | 29 | F | ½ | 135 | ..... | ..... | Trichophytid |
| 2555 | 26 | F | 7 | 157 | ..... | ..... | Eczematoid ringworm |
| 1050 | 35 | M | .. | 153 | ..... | ..... | Eczematoid ringworm |
| 2595 | 30 | M | 3 | 152 | ..... | ..... | Eczematoid ringworm |
| 2521 | 40 | M | 1 | 181 | ..... | ..... | Eczematoid ringworm |

170 mg. (maximum, 197 mg.), and seven, or 64 per cent, are normal. There appears to be no relation between cholesterol and age, sex, duration or extent of the disease.

Table 4 records the results of fifteen determinations in thirteen cases of vegetable parasitic diseases. Of the fifteen determinations, one, or 7 per cent, are above 170 mg. (i. e., 181 mg.), and fourteen, or 93 per cent, are normal.

## CONCLUSIONS

1. Of 217 determinations of cholesterol on the whole blood in 103 cases of acne, 76 per cent fall between 131 and 170 mg. per hundred cubic centimeters, and 23 per cent fall above 171 mg. Of the 103 patients, 59 per cent were normal throughout the period of observation, and 39 per cent at some time (although not consistently) were above 171 mg. Considering only the first determination on the whole group of 103 patients (including table 1 A of single determinations), the following distribution is obtained: none below 130 mg.; sixty-nine, or 67 per cent, from 131 to 170 mg.; fourteen, or 13 per cent, from 171 to 180 mg.; five, or 5 per cent, from 181 to 190 mg.; four, or 4 per cent, from 191 to 200 mg., and eleven, or 11 per cent, above 200 mg. Hence it is concluded that hypercholesteremia is not characteristic of acne vulgaris.

2. The cholesterol content of the blood does not follow clinical changes of acne vulgaris.

3. Of twenty-three determinations of cholesterol in seventeen cases of various types of seborrhea, fifteen, or 65 per cent, were normal, and seven, or 31 per cent, were above normal. Of eleven determinations of cholesterol in nine cases of psoriasis, seven, or 64 per cent, were normal, and four, or 36 per cent, were above 171 mg. Of fifteen determinations of cholesterol in thirteen cases of vegetable parasitic diseases, fourteen, or 93 per cent, were normal. Although the number of cases of the latter diseases is too few to substantiate definite conclusions, it appears probable that the diseases are not related to the cholesterol content of the blood and are not characterized by either hypocholesteremia or hypercholesteremia. It is possible that cholesterol plays a definite part in the skin in these diseases, but it is not revealed by the study of cholesterol in the blood.

# CAPILLARY PERMEABILITY IN DISORDERS OF THE SKIN

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Studies on the permeability of the skin have been undertaken in recent years in an effort to clarify a number of pathologic processes. It is but natural to inquire into the functional as well as the organic state of the walls of the blood vessels whenever abnormal exchanges occur between the tissues and the blood. With these studies it is possible to elicit information related not only directly to the skin itself and its diseases, but indirectly to the internal organs, as was shown by Müller and Petersen [1] through their demonstration of the so-called splanchnic-peripheral balance. This showed that the visceral and skin vessels are oppositely oriented as to tonus and blood content at any given moment. Petersen [2] and Gännslen [3] have further provided a simple means for studying capillary permeability of the skin by means of an artificial blister. The amount of protein escaping through a capillary wall is an index of its permeability, and this is quantitatively reflected by comparing the amount of protein in a blister to that in the blood.

## METHOD

A blister was produced by means of a cantharides plaster, and the amount of protein in the blister fluid was compared with that in the blood serum. The protein content of spontaneous blisters occurring in pemphigus, erysipelas and other diseases was similarly compared to the blood protein. Note was made also of the time required for the blister to form. We used a cantharides plaster ¾ inch (1.9 cm.) square placed just below the bend of the elbow. A smaller plaster will suffice for the drop of blister serum necessary for a determination, but we used some of the fluid for other purposes. The patients were instructed to set the plaster at 4 a. m. and to remove it at 9 a. m., unless the blister formed earlier, in which case they removed it at the time of formation. The blister was evacuated shortly after it was formed. The amounts of protein in the blister fluid and in the blood serum were estimated by first determining their refractive indexes. (The refractive index of a solution is proportional to its protein content.) Then the

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1. Müller, E. F., and Petersen, W. F.: Klin. Wchnschr. **5**:53, 1926.

2. Petersen, W. F.: Permeability of Skin Capillaries in Various Clinical Conditions, Arch. Int. Med. **39**:19 (Jan.) 1927.

3. Gännslen, M.: München. med. Wchnschr. **69**:263, 1922.

index for the blister fluid was referred to the exudate scale of the Reiss table, which gave the amount of protein contained, and the amount of protein in the blood serum was similarly determined, but the serum scale was used instead of the exudate scale. The blister time is the interval between the time the cantharides plaster is placed on the skin and the first perceptible appearance of the blister. The ratio of the percentage of blister protein to the percentage of serum protein is the permeability value, and the ratio of this permeability value to the blister time is called the inflammatory index. Thus, if the blister protein is 3 per cent and the serum protein 6 per cent, then the permeability ratio is 50 per cent; and if it takes five hours for the blister to appear, the inflammatory index is 10.

## RESULTS

Blisters in urticaria gave the lowest permeability values, while those in pemphigus gave the highest, although determinations from spontaneous blisters in the latter are not strictly comparable to those obtained with cantharides plasters. That the spontaneity of the blisters does not explain the extreme value found in pemphigus is indicated by the moderate value of the spontaneous blisters in erysipelas. It is possible, however, that the presence of inflammation is an important element to be considered. In pemphigus there was none apparent at the base of the spontaneous blister, whereas in erysipelas there was. Dermatitis herpetiformis gave values intermediate between the low ones in urticaria and the normal.

Normal values of permeability range from about 65 to 75, and the normal blister time is from five to five and one-half hours. In urticaria the values ranged from 32 to 65, and the average blister time was six and one-half hours. There were both subnormal and hypernormal permeability values in eczema, but the blister time was always short, being on the average, three and one-half hours. The average permeability in lichen planus was 56, and the blister time five and four-fifths hours. In dermatitis herpetiformis the average permeability was 63, and the average blister time five and two-thirds hours. The spontaneous blisters in pemphigus gave permeability values of 100, and in one blister induced by cantharides plaster 78, with a blister time of five and one-half hours. The blisters in all the rest of the dermatoses that were studied, such as scabies, impetigo pityroides, gave more or less normal values. Both dermatitis venenata and tuberculosis colliquativa with fever gave blister times of three hours.

## COMMENT

The permeability of the skin as deduced from a blister produced by the application of a cantharides plaster does not necessarily represent the permeability found in lesions such as wheals, but at present we have no method that directly determines the permeability of the skin lesions themselves. However, in definite disease entities such as urti-

caria, permeability values of cantharides blisters are fairly uniform and characteristic, and since such charactertistic values are found in particular entities, it is probable that the same set of conditions that determine the lesions also determine the reaction of the nearby skin free from lesions to the cantharides plaster. The blister produced by the cantharides plaster, therefore, can be assumed to show a permeability value similar to that of lesions in the process of evolution at the time that the plaster is placed.

It is commonly believed that the degree of permeability roughly parallels the intensity with which the injuring agent acts, a subject to which Osterhout [4] in particular has given attention. And further, the limited number of primary morbid morphologic forms or lesions that the skin assumes can be arranged in a series to fit a scale of degrees of injuring intensity. The ascent of this scale would commence with the production of a macule, and carry through to form at varying levels papules, bullae and other lesions, and finally gangrene. Deductions from the data in this report, however, are contrary to these common beliefs. The analyses were all made from the same type of lesion, the blister, yet there was a great difference between the permeability of the similarly appearing blisters induced in urticaria at one extreme and in pemphigus at the other.

The blood vessels in inflammation and erythema are enlarged and engorged, and thus are thought to allow greater egress of their constituent material, enabling blood elements to infiltrate the tissues more quickly and in larger quantities than occurs under normal circumstances. The data in our experiments seem to discourage this belief, since normal persons showed a degree of permeability about midway between the extremes of the spontaneous blisters in pemphigus and the blisters induced by a cantharides plaster in urticaria. It is during the height of an urticarial attack that the permeability of the skin vessels is lowest, and, contrariwise, the return to normal ushers in a rise in permeability which gradually approaches normal.

Stasis is perhaps the most important consequence of the constriction of the arterioles and capillaries in the production of the wheal. The slowing or complete stoppage of the blood stream causes an accumulation of carbon dioxide and an increase of acidity in the serum. At the same time, stasis causes a loss of water from the blood into the tissues, which may amount to as much as 30 per cent of the total water of the blood serum; [5] the blood proteins that are held back in the vessels become concentrated with a consequent partial loss of the blood's alkaline reserve.

4. Osterhout, W. J. V.: Injury, Recovery and Death, Philadelphia, J. B. Lippincott Company, 1922.

5. Dautrebande, L.; Davies, H. W., and Meakins, J.: Heart **19**:133, 1923. Peters, J. P.; Bulger, H. A.; Eisenman, A. J., and Lee, C.: J. Biol. Chem. **67**:176, 1926.

Tonus of the blood vessels is another factor to be considered in the evolution of lesions, and is reflected, in the induced blister, by the time it takes for the blister to form. Undoubtedly, the predominant factor determining the tonus of the blood vessels is the condition of the autonomic system. When the parasympathetic system predominates over the sympathetic, the arterioles are relaxed, and the blister time is short. Whenever the blister time is longer, the arterioles are contracted, with the sympathetic system predominating over the parasympathetic.

Urticaria was the first dermatosis that we studied. In this we found an altered permeability that was very low, just opposite to that which we had expected. A paradoxical reaction, besides the apparent inconsistency of the increased volume of exudate and the decreased permeability to be found in urticaria, is that produced by epinephrine. In urticaria it acts opposite to the way it does usually. Under ordinary circumstances, epinephrine causes a diminished permeability, and we have found that the passage of the urticarial state is coincidental with an increase in permeability. However, in urticaria the vessels of the skin are probably in a specially altered state so that paradoxical response should be no surprise. The usual response in most persons to an injection of epinephrine is a rise in the blood pressure; however, in urticaria and asthma and other allergic states, there is a fall in blood pressure when epinephrine is used. Likewise, in bronchial asthma, epinephrine produces a dilation of the bronchi, whereas, in normal persons, it contracts the bronchi. Cells vary from time to time in their responses to the same hormone, depending on their ionic milieu, the hydrogen ion concentration and the calcium-potassium balance. And that which is concerned in the variation in response of the cells or vessels to hormones probably applies also to nerve impulses and drugs. Be that as it may, this paradoxical response of the vessels of the skin to epinephrine in urticaria must await more complete information before it can be entirely explained.

Another condition that we studied was dermatitis herpetiformis. Although we found the permeability distinctly reduced below normal, it was not quite so low as that which we found in urticaria. It is interesting, too, that arsenic has long been found useful empirically in dermatitis herpetiformis, and that it has been found that the administration of arsenic increases the permeability. An increase in permeability, according to our limited observations, goes hand in hand with clinical improvement in dermatitis herpetiformis.

Persons with lichen planus are generally somewhat unstable and fall within the group that is easily sensitized. They are often victims of asthma or hay fever, or members of families subject to these maladies. It is therefore not surprising that, like that in urticaria, the permeability

in lichen planus should be reduced. However, the permeability in lichen planus is not as low as that in urticaria.

We were fortunate to have the opportunity to make observations on persons in whom bullae developed without any grossly demonstrable inflammation. These included subjects with pemphigus vulgaris and one in whom a bulla developed by mechanical means. Only young bullae were used in the determinations for pemphigus, because the values change with the age of the bullae. In our series the protein in the spontaneous blisters of pemphigus was found to be equal to that of the blood serum. This indicates that there was no selective permeability on the part of the vessels, since they allowed even the largest protein molecules to pass through. It is probable that the blister content in pemphigus does not come from the blood vessels directly, but from the fluid of the interstitial areas. A blister produced by a cantharides plaster on one of the subjects with pemphigus yielded a permeability value less than that of the spontaneous blisters, but distinctly higher than the normal. An illuminating observation was made on a man whose hand had been pinched in closing a door and in whom soon afterward a bulla developed at the site of trauma. We were able to obtain the contents of this bulla and to compare its protein content with that of the blood serum. Both were found to contain an equal amount of protein. In this case there was a mechanical shearing of one layer of the skin from another. This laid open lymph spaces, and the lymph collected in a pool. It is possible that in pemphigus the bullae result from a fragility of certain areas of interstitial tissue. Whether an examination of the permeability changes in pemphigus will be of any value in differential diagnosis remains to be seen. None of our patients with dermatitis herpetiformis had vesicles large enough to be of use in determining the permeability. However, in pemphigus the blisters induced by cantharides plasters showed permeability values definitely higher than those in dermatitis herpetiformis. We had no opportunity to examine spontaneous blisters in erythema multiforme to see if such observations on permeability might be used in distinguishing between pemphigus and erythema multiforme.

Various combinations of the degree of permeability and the length of blister time may be present. Thus, an increased permeability may be present with a decreased blister time. This was found, for example, in a case of dermatitis venenata in which the degree of permeability was 80, while the blister time was three hours. On the other hand, with a decreased permeability, there may be a lengthened blister time, which does not necessarily mean a change of the capillary wall, since a change in the internal capillary pressure could account for this combination. This was found in the active cases of lichen planus, dermatitis herpeti-

formis and urticaria. But the permeability and blister time need not necessarily be reciprocals of one another in the matter of degree and time. Thus, in a case of infectious eczematoid dermatitis the permeability ratio was 75 per cent, while the blister time was seven hours. On the other hand, in a case of eczema with asthma, the permeability was 52 per cent, while the blister time was also low, three hours.

The degree to which current conditions may affect the patient is exemplified by one of the patients with eczema, who said that every time she became feverish, as during a coryza or when she had a sore throat, the condition of her skin improved. During one of these colds, the permeability, which had previously been low, became 83 per cent, while the blister time remained short, three and one-half hours, just one-half hour longer than it had been before. During fever, there is a tendency for a partial acidosis to develop, which would influence a subject with eczema from a parasympathetic toward a sympathetic orientation. Calcium therapy causes the same partial acidosis.

## SUMMARY

1. The blister method of studying permeability is described.

2. The relation of the degree of permeability to the inflammatory index is given.

3. The results obtained from the use of the blister method are briefly summarized.

4. An attempt was made to analyze and interpret some of the probable factors responsible for changes in permeability in some dermatoses.

# BACTERIOLOGY OF THE INTESTINE AND BLOOD IN PSORIASIS

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In this paper a description is given of the bacteriologic observations for the stools and blood in a series of cases of psoriasis. For the most part the patients were in attendance at the dermatology division of the Cornell Clinic. A brief preliminary report on the intestinal flora in twenty of these cases has been published,[1] but in the present communication the data for the complete series of thirty cases are given in detail. The purpose of this study was to determine if the intestine or blood during any stage of this skin disease might harbor bacterial or mycotic organisms of such a character as to suggest an infection, intoxication or sensitization of the skin from these sources. Although it cannot be said that our results have shed any positive light on the etiology of psoriasis, it seems worth while to put them on record in some detail, for to our knowledge the intestinal flora in this disease has not been studied heretofore along these lines. Many theories attempting to explain the disease have been suggested, but none has found wide acceptance or has been adequately supported by experimental proof. The ultimate solution of this problem seems obviously to be dependent on its study from every point of view with the hope that a promising lead may emerge. With this thought in mind the investigation reported here was undertaken.

## CLINICAL DATA

In table 1 a brief clinical history is given for each of the thirty consecutive cases. It may be noted that the series includes patients from 16 to 60 years of age exhibiting various degrees of duration, acuteness and extent of the disease. The examinations were made during the colder months, viz., from November to April, when the disease is generally more active than in the summer.

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1. Schwartz, H. J.; Torrey, J. C., and Fraser, J. F.: Intestinal Flora in Psoriasis, A Preliminary Report, Arch. Dermat. & Syph. **23**:70 (Jan.) 1931.

### EXAMINATIONS OF STOOLS

The evening before the collection of the fecal specimen each patient was instructed to take a 1 grain (0.065 Gm.) tablet of phenolphthalein and to bring to the laboratory promptly, in a sterile container, a sample of the softer portion of the stool. The bacteriologic examination was started as soon as possible after receipt of the specimen. Most of the cultural methods employed in this study have been described by one of us (Dr. Torrey) in previous papers,[2] and only additional procedures are noted in this paper.

TABLE 1.—*Clinical Data for Thirty Patients*

| Name | Age | Duration | Extent |
|---|---|---|---|
| 1. J. R. | 59 | 10 years | Acute exacerbation on chest and back |
| 2. A. G. | 28 | 1 year | Scalp |
| 3. J. S. | 18 | 1½ years | One large plaque on left outer calf; other small lesions |
| 4. B. B. | 38 | 3 years | Generalized, with typical patches on knees and elbows |
| 5. T. H. | 29 | 14 years | Nearly generalized lesions from size of pinhead to that of shilling |
| 6. G. G. | 33 | Several | Lesions on elbows and one hand |
| 7. H. H. | 47 | 25 years | Lesions on trunk and extremities |
| 8. E. J. | 45 | 3½ years | Scattered lesions on trunk, elbows and knees |
| 9. C. McD. | 30 | 4 months | Trunk and legs, scattered |
| 10. J. R. | 49 | 24 years | Extensive on trunk and extremities |
| 11. L. L. | 16 | 6 years | Thick, scaling lesions; scalp, back and arms |
| 12. N. W. | 43 | 7 years | Practically universal; itching acute type |
| 13. P. W. | 25 | 5 years | Lesions on scalp and body; some large |
| 14. H. W. | 58 | 10 years | Scattered, generalized |
| 15. F. A. | 32 | 9 months | Lesions behind ears and over elbows |
| 16. W. P. | 19 | 14 years | Acute generalized, confluent patches on face |
| 17. M. O. | 59 | 8 years | Trunk, scalp and extremities; worse in cold weather |
| 18. M. B. | 42 | 2 years | Scalp and elbows |
| 19. B. M. | 32 | 2 years | Scalp |
| 20. A. B. | 49 | 5 years | Lesions on wrists, elbows, knees and hands |
| 21. B. Ba. | 65 | 20 years | Trunk and limbs |
| 22. M. DeP. | 36 | 15 years | Trunk, limbs and scalp |
| 23. D. M. | 31 | 8 years | Trunk, limbs and face |
| 24. J. C. | 27 | 15 years | Scalp, trunk, extremities and nails |
| 25. E. C. | 31 | 7-8 years | Scalp, elbows, knees, back |
| 26. B. M. | 32 | 6-7 years | Scalp, trunk, limbs |
| 27. C. McA. | 40 | 30 years | Generalized guttate type with widely scattered numerous guttae |
| 28. R. W. | 24 | 10 years | Thick scaly patches in a girdle form around waist and on scalp |
| 29. M. O. | 26 | 6-7 years | Scalp and extremities |
| 30. M. A. | 34 | 12 years | Typical patches scattered over body |

In twenty-two instances the fecal specimens were normal in appearance and general character; in five they were foul and fluid or mushy, and in the remaining three, of a marked fermentative acid type. The reactions in twenty specimens were within the usual range of from about $p_H$ 6.4 to 7.4; two were markedly acid ($p_H$ 5.6 to 5.8) and two very alkaline ($p_H$ 8.4). Three showed abnormal amounts of mucus; in two of these the odor was foul and in one strongly acid. About the same findings might be expected in a similar series of unselected non-

2. Torrey, J. C.: A Comparatively Simple Technic for the Bacteriologic Study of Fecal Material, J. Infect. Dis. **39**:351 (Nov.) 1926. Torrey, J. C., and Montu, E.: The Influence of an Exclusive Meat Diet on the Flora of the Human Colon, J. Infect. Dis. **49**:141 (Aug.) 1931.

psoriatic cases, and there was, accordingly, nothing distinctive for this disease in the character of the fecal specimens.

*Bacterial Counts.*—Direct microscopic examination of gram-stained fecal films prepared as described in a previous article [3] in accordance with a standardized technic showed an average in seventeen of these cases of 57 bacteria per field, with a range of from 20 to 108 bacteria. In three normal adults on a normal diet rather high in carbohydrates the average counts for three examinations each were, respectively, 134, 103 and 48. These direct counts, which included both living and dead bacteria, certainly do not indicate the presence of larger numbers of bacteria in the intestine in psoriatic than nonpsoriatic patients, but rather the contrary. Only an occasional specimen showed spirochetes or mycotic organisms. The count for bacterial spores was rather below that commonly observed.

The quantitative estimates for viable aerobic bacteria, capable of growth on the surface of the bromcresol purple lactose agar plates at 37 C., as indicated by colony counts, showed a range of from very few to innumerable bacteria per standard loop of fecal dilution 2. The vast majority of the colonies were formed by members of the colon and enterococcus groups. There were seven very high counts and thirteen very low ones, with the remainder ranging between these limits.

*Colon Group.*—The Ayers and Rupp [4] agar medium plates permitted more exact quantitative determinations for Bacterium coli. The counts were all estimated for 1 cc. of dilution 3, viz. $10^2$, of the primary stool suspension. There were six cases with B. coli counts below 100, nine between 100 and 1,000, seven between 1,000 and 10,000 and eight with more than 10,000. The corresponding B. coli counts for fourteen normal (nonpsoriatic) adults on unrestricted diets, ranging in age from about 20 to more than 60 years, showed, for 1 cc. of the corresponding fecal dilution: one count below 100, five between 100 and 1,000, four between 1,000 and 10,000 and four more than 10,000. Davidson,[5] in a carefully conducted comparative study of the fecal flora of normal adults and of those suffering from various pathologic conditions, reported for the twenty-six normal persons B. coli counts of from 50 to 500 per cubic centimeter of his fecal dilution 3. This dilution was apparently slightly lighter than our dilution 3. His normal subjects were all athletes and heavy eaters of meat. From the foregoing data it may be observed that the average B. coli count for these cases of psoriasis was

3. Torrey and Montu (footnote 2, second reference).

4. Ayers, S. H., and Rupp, P.: A Synthetic Medium for the Direct Enumeration of Organisms of the Colon-Aerogenes Group, J. Bact. **3**:433, 1918.

5. Davidson, L. S. P.: The Gastro-Intestinal Flora in Pernicious Anemia, J. Path. & Bact. **31**:557, 1928.

somewhat higher than for Davidson's normal series, but did not differ materially from our observations for a series of unselected normal adults. Further, psoriasis may evidently develop as readily in persons exhibiting an extremely low B. coli count as in those with unusually high counts. In fact, in one of our cases (case 23) no B. coli were found, the flora being composed almost exclusively of anaerobic organisms. The B. coli strains isolated from these cases of psoriasis were subjected to various differential tests to determine if any particular types as regards virulence or biochemical properties were associated with this disease. This was found not to be the case. Only six of the patients harbored hemolytic B. coli, and practically all of these strains produced no more than a narrow zone of hemolysis when streaked on plain blood (rabbit) agar. Dudgeon, Wordley and Bawtree,[6] in 1922, discussed fully the significance and characteristics of hemolytic B. coli. They demonstrated that the hemolytic types constitute serologically a more homogeneous group than the nonhemolytic types, and that apparently they have in general greater invasive properties. It has also been the experience of Dudgeon that hemolytic B. coli are found in large numbers more frequently in the presence of colonic inflammation than when the intestinal mucosa is in a normal condition. They are, however, by no means restricted to the abnormal colon, as is indeed indicated by their distribution in these thirty cases: The three stool specimens with excessive mucus yielded nonhemolytic B. coli alone, whereas five of the six specimens positive for the hemolytic type were not obviously abnormal. The colon strains isolated from twenty-five of these cases were tested for virulence by intraperitoneal inoculation of white mice with standardized dosages of twenty-four hour plain broth cultures. From a very extensive experience on the part of one of us [2] it has been concluded that a strain of B. coli that kills a mouse within from twenty-four to forty-eight hours following intraperitoneal inoculation with 0.033 cc. exhibits definite virulence. In only one case were B. coli of noteworthy virulence found; in nine cases strains of only slight virulence were recovered, and in the remainder the colon type was avirulent. The colon strains from thirteen of the cases were strong indol producers; from fourteen cases they were moderate to slight producers, and from three they were negative for indol. All of the facts reported indicate that strains of B. coli vegetating in the colon of this series of cases of psoriasis vary in character in about the same way and degree that one might expect to find in a similar series of normal persons. Paracolon types, viz., aberrant members of the colon

6. Dudgeon, L. S.; Wordley, E., and Bawtree, F.: On Bacillus Coli Infections of the Urinary Tract Especially in Relation to Hemolytic Organisms, J. Hyg. **21**:168, 1922-1923.

group which split lactose very slowly or not at all, were encountered in only one case, and the same was true for the mucosus group including B. aerogenes.

*Proteolytic Gram-Negative Aerobic Bacilli.*—The principal intestinal representatives of this group are B. proteus and B. pyocyaneus. The former was found only once and the latter not at all. These types are restricted largely to putrefactive floras in stool specimens of marked alkalinity.

*Streptococcus Group.*—In the classification of the streptococcal types isolated from these stool specimens, a distinction was made between buccal types and intestinal types or enterococci, principally on the basis of the ability of the latter to split esculin. Distinctive morphology, fermentation of mannitol and ability to grow in bile peptone broth also served in part to differentiate the two groups. Definitely buccal types of streptococci were recovered from the stools in only seven cases. These were long, chain-forming, alpha prime or alpha varieties which were negative for mannitol and, for the most part, positive for raffinose. No representatives of Streptococcus haemolyticus were found. In fourteen cases there were relatively few enterococci of any type and in eleven cases moderate numbers, and in only five cases did they outnumber B. coli. Except for the few cases showing chain-forming types, there was no unusual streptococcus element in the flora and no suggestion of cutaneous infection or sensitization from that source.

*B. Acidophilus.*—Only three, or 10 per cent, of the thirty cases of psoriasis showed B. acidophilus by cultural methods as an element in the fecal flora. This is an unusually small percentage. In a series of fifteen normal adults examined by one of us [2] some years ago, in which series acid whey agar was also used as a plating medium, B. acidophilus was found to be present in considerable numbers in the stools in six, or 40 per cent. These persons were taking an ordinary unrestricted diet. Sanborn,[7] in a recent study of the fecal floras of adult psychopathic patients on a diet rather high in carbohydrate and low in animal protein, has reported that eighteen of the twenty-six subjects, or 70 per cent, showed B. acidophilus as an element in the flora in numbers ranging from 10 to 90 per cent of the total viable aerobic bacteria. In these determinations she employed casein digest agar, of $p_H$ 6.8 to 7.0, with a carbon dioxide atmosphere, which, as Kulp [8] has shown, greatly favors the growth of B. acidophilus, particularly the X type. Making due

7. Sanborn, Agnes G.: The Fecal Flora of Adults, with Particular Attention to Individual Differences and Their Relationship to Effects of Various Diets. I. The Individual Differences on Normal Diet, J. Infect. Dis. **48**:541 (June) 1931.

8. Kulp, W. L.: An Agar Medium for Plating L. Acidophilus and L. Bulgaricus, Science **66**:512, 1927.

allowance for the factor of technic, it would appear that a peculiarity of the fecal floras of this series of cases of psoriasis lies in the dearth of B. acidophilus. We hesitate, however, to attach any significance to this observation, particularly as two of the three positive cases yielded fairly high counts. Only the Y type was found.

*Yeastlike Fungi.*—In view of the recent suggestion of Wachowiak and his coworkers[9] that moniliae might in some way be related to psoriasis, determinations of the presence or absence of yeastlike fungi in the stools of these patients were made. Sabouraud's agar medium was used, and surface-seeded streak plates were prepared from the undiluted fecal material and dilution 1. Yeastlike organisms were found in twenty of the thirty specimens, but generally only a few colonies on a plate—only six, or 20 per cent, showed fifty or more colonies per small loop of fecal material. This is about what one might expect in a series of normal persons. The isolated strains were examined carefully for formation of hyphae. The cultures that did not exhibit this characteristic when growing in semisolid agar were seeded on Czapek agar as modified by Thom and Church.[10] Only ten of the thirty cases showed hyphae-forming monilia. Nye, Zerfas and Cornwell,[11] as a result of culturing one hundred and ninety-two stools from one hundred and twenty-one persons suffering from one or another of a great variety of diseases, isolated yeastlike fungi from fifty-one cases, or 42 per cent, but in only 15 per cent were ten or more yeast colonies found on the first or most heavily seeded culture plate. There is thus a fairly close correspondence with our small series. Among their positive cultures, however, there was an overwhelming predominance of types of moniliae, particularly Parasaccharomyces A, whereas in a third of these cases of psoriasis the nonhyphae yeast type, Cryptococcus, alone was found. Nine of the moniliae recovered were subjected to differential fermentation tests, and two were found to correspond to Parasaccharomyces A, three to B, two to C and two to G. Thus no evidence was secured in support of the theory of Wachowiak and his associates[9] that a general sensitization of the skin might result through absorption of moniliae or their products from the intestine. These investigators have reported the presence of Monilia in the feces in 86 per cent of a series of fifty-six cases of psoriasis, as con-

9. Wachowiak, W.; Stryker, G. V.; Marr, J.; Bock, H., and Fleisher, M. S.: The Occurrence of Monilia in Relation to Psoriasis, Arch. Dermat. & Syph. **19**: 713 (May) 1929.

10. Thom, C., and Church, M.: The Aspergilli, Baltimore, Williams & Wilkins Company, 1926.

11. Nye, R. N.; Zerfas, L. G., and Cornwell, M. A.: The Presence and Importance of Yeast-Like Fungi in the Gastro-Intestinal Tract in Pernicious Anaemia, Am. J. M. Sc. **175**:153, 1928.

trasted with the 33.3 per cent of our thirty cases. Although they did not give quantitative estimates, they admitted that in some of the cases this organism was demonstrated with considerable difficulty. Using the same methods, however, in a series of normal persons, they were able to find Monilia in the stools of only 6 per cent.

*Anaerobic Flora.*—Dependence was placed principally on cultures of the fecal dilutions in cooked meat medium for a quantitative and, to some extent, qualitative study of the spore-bearing anaerobes in the stools from these cases of psoriasis. Subcultural procedures, adequate for the identification of B. welchii, permitted an estimation of their approximate numbers for each patient. Two cases were negative for this organism; in six cases the highest positive dilution was no. 1; in nine, no. 2; in eight, no. 3, and in five, no. 5. In 80 per cent of these cases the highest positive fecal dilution was not above no. 3, and in about 56 per cent, not above no. 2. The results are about what one might expect in a series of normal adults according to the experience of one of us,[2] and, in fact, correspond very closely to Davidson's [5] findings for twenty-six normal adults. He reported that in twenty-two (84.6 per cent) the highest positive dilution for B. welchii was not above no. 3, approximately equivalent to dilution 3. Of the remaining four cases, three were positive for no. 5 and one for no. 7.

In the great majority of these cases of psoriasis B. welchii was the predominant spore-bearing anaerobe in the stool. Aside from B. histolyticus, which is a rarity in the human intestine, the only other gram-positive spore-bearing anaerobes that digest this cooked meat medium actively are B. sporogenes, B. bifermentans and Cl. putrificum. B. sporogenes is the most active of all and in seven days causes a decrease in height of the meat column of 1.5 cm. or more. There were only three cases in this series in which this organism was apparently active and only seven in which the digestion of the cooked minced meat caused the lowering of the column in a tube seeded with heated fecal suspension as much as 1 cm. or more.

A few cultures of the whole flora on dextrose blood agar plates under conditions of reduced oxygen tension were carried out. In one case (case 23) almost the whole flora was found to consist of nonspore-bearing anaerobic organisms, mostly streptococci and gram-positive rods, some of which were apparently accountable for the foul odor of the feces. As this finding was unique, however, it was without apparent significance as far as the skin disease was concerned.

Some years ago one of us [2] suggested the use of cooked meat medium for the determination of the presence and activity of proteolytic spore-bearing anaerobes in fecal floras from both the quanti-

tative and the qualitative standpoint.[12] The medium was prepared in accordance with Robertson's original formula, except that 1 per cent peptone was added. Recently Leonard and Feirer [13] adopted this method, with some modifications, as a means for titrating the degree of intestinal putrefaction. The method serves as a quantitative gage solely of the proteolytic spore-bearing anaerobes, viz., those capable of attacking and liquefying native proteins with the production of foul odors, and does not reveal the presence or indicate the activity of bacterial types, such as B. proteus and B. coli, that are capable of attacking the intermediate products of protein decomposition and that are responsible in whole or in part for the fouler odors associated with intestinal putrefaction. On the basis of their classification, Leonard and Feirer concluded that the fecal specimens from one hundred and twenty-seven subjects gave evidence of none or of only slight putrefaction in about 50 per cent of instances; the stools of about 33 per cent showed no more than moderate putrefactive properties, and those of about 20 per cent showed pronounced putrefactive properties. When this method of classification is applied to the cultural findings for this series of thirty cases of psoriasis we find that twenty-three, or approximately 77 per cent, would be considered as showing no more than slight putrefactive properties, three, or 10 per cent, moderate putrefactive properties, and four, or about 14 per cent, marked or pronounced putrefactive properties. Allowing for certain differences in the technic, particularly the fact that only one fecal specimen was examined from each case, our observations are quite similar to those reported by Leonard and Feirer, and we may conclude that these examinations give no evidence of unusual numbers of proteolytic anaerobes in the colons of sufferers from psoriasis; in fact, quite the contrary.

### BLOOD CULTURES

There is a possibility of a bacterial or mycotic allergic factor being concerned in the etiology of psoriasis. On the basis of such a theory it might be supposed that the skin had become sensitized to such foreign proteins and that the active pathologic process is the result of absorption of micro-organisms from the intestine, buccal cavity or elsewhere to which sensitization had been acquired. In fact, Wachowiak and his associates,[9] as has been mentioned, recently suggested that moniliae may be related in some such way to the disease. Although this allergic theory, as far as infection is concerned, is as yet inadequately supported by positive evidence and seems to lack plausibility, it was deemed desir-

12. Torrey (footnote 2, first reference).

13. Leonard, V., and Feirer, W. A.: Dihydranol, Bull. Johns Hopkins Hosp. **48**:25, 1931.

able to put it to the test by careful blood cultures in our series of psoriasis cases. Accordingly such cultures were made for sixteen patients; twelve of these were among those for whom examinations of the stools were carried out, and four were additional to that series. The technic was essentially that employed by Cecil, Nicholls and Stainsby [14] in their study of the bacteriology of chronic infectious arthritis. In making subcultures from the primary broth cultures, rabbit-blood agar poured plates, seeded with 0.1 cc. of the blood broth cultures, were prepared, and also in many instances dextrose hormone agar or purple lactose agar plates, surface-seeded with the same amount of the culture in order to control the possibility of contamination from the rabbit blood. These platings from the original blood cultures in the two bottles were prepared every five or ten days, or until a positive growth was obtained or about thirty days' incubation had elapsed.

TABLE 2.—*Cases of Psoriasis Yielding Positive Blood Cultures*

| Case | Extent of Lesions | Bacteria Isolated | Incubation Period of Blood Culture | Probable Source of Bacteria |
|---|---|---|---|---|
| 19 | Scalp | Streptococcus (alpha prima).... | 19 days | Buccal |
| 24 | Generalized | B. coli (hemolytic)..... | 4 days | Intestinal |
| 27 | Generalized | Streptococcus (alpha) ..... | 5 days | Buccal |
| 29 | Generalized, developing | First examination, 4/11/31, enterococcus (gamma) | 10 days | Intestinal |
| | | Second examination, 5/2/31, streptococcus (alpha) | 3 days | Intestinal |
| 33 | Developing case | Gram-positive diplococcus (unidentified) | 15 days | ? |

Before the primary culture was discarded a plating was made on Sabouraud agar for yeastlike fungi. Colonies developing in these subculture plates were identified by suitable bacteriologic procedures. Staphylococcus albus was the organism that most frequently developed in the blood cultures, but this was considered a contamination.

Of the total of sixteen cases of psoriasis in which the blood was cultured, eleven yielded negative results. These patients were those in cases 8, 16, 17, 22, 23 (twice), 25, 28, 30, 31, 32 and 34. For the last three, examinations of the stools had not been made. The observations for the five cases yielding what were considered to be positive blood cultures are given in table 2.

Cecil, Nicholls and Stainsby,[14] using essentially the same cultural method, have reported the isolation of a streptococcus from the blood in forty-eight, or 61.5 per cent, of seventy-eight cases of chronic infectious arthritis, and 83.3 per cent of these strains exhibited marked

14. Cecil, R. L.; Nicholls, E. E., and Stainsby, W. J.: The Bacteriology of the Blood and Joints in Chronic Infectious Arthritis, Arch. Int. Med. **43**:571 (May) 1929.

similarities both culturally and serologically and have been tentatively designated as an attenuated Streptococcus haemolyticus. Fifty-four control cases, including cases of degenerative arthritis, gonococcal arthritis and a considerable variety of other pathologic conditions, for which the blood was cultured by the same method, all yielded sterile cultures. Two of the cases of chronic infectious arthritis were complicated by psoriasis, and from these the typical strain was isolated from the blood. In our series of cases of psoriasis in which blood cultures were made none yielded this hemolytic streptococcus. On the other hand, five cultures, or 31.3 per cent, were positive for some other organism, aside from white staphylococci, and in the three cases from which streptococci were isolated, they were of the alpha (viridans) or alpha prima type. Comparison of these observations with the controls of Cecil, Nicholls and Stainsby suggests that bacteria from the buccal cavity (as in two cases) or from the intestine (as in two and possibly three cases) are more apt to invade the blood stream in psoriasis than in some other pathologic conditions in which infection of the blood has not been definitely established. It is of interest that in one case (case 29) in which two blood cultures were made, three weeks apart, both cultures yielded intestinal types of streptococci. On the other hand, the bacteria recovered from the blood were heterogeneous in type, were apparently present in exceedingly small numbers and seemed to represent fortuitous invaders which were caught by chance in the 20 cc. of blood submitted for culture in each case. Further cutaneous sensitization tests were practically negative for the several strains recovered from the blood. No yeastlike fungi were recovered from the blood in any case. Wachowiak and his associates,[9] however, have reported the isolation of Monilia from the blood in 17 per cent of their series of fifty-six patients with psoriasis. Our failure to confirm their observations may have been due to differences in the technic employed.

### INTRADERMAL INOCULATION TESTS

Intradermal injections were made with antigens prepared from bacterial cultures recovered from ten of these cases of psoriasis, including intestinal, and when they were available, blood strains. In the preparation of the antigens the Famulener technic was employed, which briefly is as follows:

Twenty-four hour growths on agar slants are evenly suspended in about 10 cc. of sterile solution of sodium chloride and filtered through sterile absorbent cotton. The filtrate is then centrifugated in a Hopkins' vaccine tube for one-half hour (2,800 revolutions per minute). The bacterial sediment packed in the narrow graduated end is then made up to a 1 per cent suspension (0.01 cc. packed cells in 0.99 cc. solution of

sodium chloride). This suspension is heated at 60 C. for one-half hour and tested for sterility. If the suspension is sterile, cresol U. S. P. is added (0.25 per cent). The dosage for the intradermal test is 0.01 cc., and the test is controlled at another site on the arm by the injection of 0.01 cc. of cresol-saline diluent. The skin reactions generally reach their height within from twenty-four to forty-eight hours, but the sites of inoculation should be observed for three days.

In table 3, which gives the details of these cutaneous sensitization tests, the maximum reaction, characterized by marked erythema and swelling at the site of inoculation, together at times with pain in the

TABLE 3.—*Cutaneous Reactions to Bacterial Antigens*

| Case | Antigen | Organisms | Source | Skin Reaction |
|---|---|---|---|---|
| 16 | 1 | B. coli (communior) | Intestine | 0 |
| | 2 | Enterococcus (viridans) | Intestine | 0 |
| 19 | 1 | Streptococcus (gamma) | Blood | 0 |
| 17 | 1 | Enterococcus (viridans) | Intestine | 1+ |
| | 2 | M. zymogenes | Intestine | 1+ |
| 22 | 1 | B. coli (communior) | Intestine | 4+ |
| | 2 | Enterococcus (viridans) | Intestine | 0 |
| 24 | 1 | B. coli (communis) | Intestine | 2+ |
| | 2 | Enterococcus (viridans) | Intestine | 0 |
| | 3 | B. coli (haemolyticus) | Intestine | 0 |
| 25 | 1 | B. coli (communior) | Intestine | 2+ |
| | 2 | Enterococcus | Intestine | 0 |
| | 3 | Streptococcus (alpha) | Blood (?) | 2+ |
| 26 | 1 | B. coli (lactici-acidi) | Intestine | 4+ |
| 27 | 1 | B. coli (lactici-acidi) | Intestine | 4+ |
| | 2 | Paracolon (anaerogenes) | Intestine | 0 |
| | 3 | Enterococcus (a) | Intestine | 0 |
| | 4 | Enterococcus (b) | Intestine | 0 |
| 28 | 1 | B. coli (communior) | Intestine | 1+ |
| | 2 | B. coli (aerogenes) | Intestine | 4+ |
| 29 | 1 | B. coli (lactici-acidi, hemolysis) | Intestine | 3+ |
| | 2 | B. coli (lactici-acidi, no hemolysis) | Intestine | 4+ |
| | 3 | Enterococcus (gamma) | Intestine | 0 |
| | 4 | Streptococcus (gamma) | Intestine | 1+ |
| | 5 | Enterococcus (gamma) | Blood | 1+ |
| | 6 | Streptococcus (gamma) | Blood | 1+ |
| | 7 | Streptococcus (alpha) | Blood | 1+ |

arm, is indicated by a 4 + symbol, and the mildest positive reaction, viz., an area of erythema from 1 to 2 cm. in diameter without tissue swelling or local pain, by 1 +. The symbols 2 + and 3 + signify intermediate reaction, with 0 indicating no reaction.

As is shown in table 3, the only marked skin reactions resulted from the injection of certain B. coli antigens, but in some other instances the response to autogenous B. coli was from moderate to negative, and to the streptococci from whatever source, from moderate to negative. Thus no positive evidence was forthcoming that in psoriasis there develops a significant cutaneous sensitization to intestinal bacteria. It seems not unlikely that the severe reactions following the intradermal injection of certain of the B. coli antigens were due to the greater toxicity of the bacterial protoplasm of these particular strains rather

than to an acquired allergic skin condition specific for the colon bacillus protoplasm as such. This was, in fact, clearly true for case 29. The B. coli antigen (no. 2), which caused a very severe local reaction in this patient and in six other psoriatic patients, produced an equally marked reaction when injected into the skin of four nonpsoriatic persons. It is of interest to note incidentally that this B. coli strain did not give a result of positive virulence on intraperitoneal injection into white mice, nor did the other B. coli antigens that produced 4+ cutaneous reactions. These findings tend to substantiate the opinion that in the colon group there are toxic and infective (invasive) strains, and that these attributes are independent and not necessarily associated.

The streptococcus antigens, including the typically intestinal type (enterococcus), isolated from the stools in seven cases and from the blood in two and possibly three cases, produced mostly mild cutaneous reactions or none at all. The common intestinal type producing methemoglobin on blood agar (Streptococcus fecalis) yielded negative results when autogenous antigens were tested on the skin in five cases, as did also an indifferent (gamma) enterococcus in one case. The streptococci, whether derived from the stools or blood, showed no more than 1+ or 2+ reactions in the three cases. These strains were of the indifferent (gamma) or viridans (alpha) types, and the slight cutaneous reactions produced by certain of them would seem to be of no significance. One of the autogenous streptococcus antigens giving a fairly marked skin reaction (case 25, no. 3) was isolated from the blood culture, but some doubt was felt as to its derivation from the blood.

Dorst and Morris[15] have reported a series of cases exhibiting various types of intestinal disability in which the patients were given intradermal inoculations with autogenous antigens prepared from one or another of a considerable variety of intestinal bacteria. The most marked reactions followed the use of B. coli antigens. They interpreted these reactions as being broadly allergic, and concluded that they were generally associated with a history of gastro-intestinal disturbances of one type or another. Famulener and Davis[16] in a similar study also noted this association but did not commit themselves to any definite theory as regards the nature of the sensitiveness exhibited, the test being applied more as a guide to vaccine dosage. Our findings, however, show that severe local reactions following intradermal inoculations with autogenous intestinal antigens, particularly B coli, may occur in persons who are essentially normal as far as the functioning of the

15. Dorst, S. E., and Morris, R. S.: Bacterial Hypersensitivity of the Intestinal Tract, Am. J. M. Sc. **180**:650, 1930.

16. Famulener, L. W., and Davis, J. S.: Skin Reactions Following Intradermal Injections of Vaccines Prepared from Intestinal Bacteria. A Preliminary Report, J. Bact. **19**:29, 1930.

gastro-intestinal tract is concerned. In interpreting these skin reactions we believe that they may quite as well be considered as reactions to a bacterial toxin in which individual susceptibility may or may not be a significant factor as a manifestation of sensitivity to foreign proteins.

## SUMMARY AND CONCLUSIONS

A report has been given on intestinal flora in thirty cases of psoriasis and on blood cultures in sixteen cases. The observations indicate:

1. The types of bacteria vegetating in the intestine in such cases, as revealed by examinations of the stools, do not differ essentially either qualitatively or quantitatively from what might be encountered in a similar series of nonpsoriatic persons who are not sufferers from gastro-intestinal disabilities. There was no evidence, so far as could be judged from the bacterial types encountered, that any unusual bacterial toxin of a soluble nature or toxic product from bacterial decomposition is formed in the intestinal tracts of sufferers from this skin disease.

These examinations did not reveal unusual numbers or types of yeastlike fungi in the stools. Moniliae occurred irregularly and always in small numbers.

2. Blood cultures were negative in eleven of sixteen cases. In the five cases with positive cultures bacteria apparently of intestinal or buccal origin were isolated, but these were diverse in type and evidently merely casual invaders of the blood stream.

3. Intradermal inoculations were made with autogenous antigens prepared with cultures isolated from the stools or the blood in ten cases. There was no evidence of sensitization of an allergic nature to the test bacteria in these cases of psoriasis.

# PERSISTENT INFECTION OF THE TONGUE DUE TO MONILIA BRONCHIALIS

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There have been few reports of infections of the tongue due to Monilia. Practically all such cases have occurred in conjunction with some other form of infection. Engman and Weiss,[1] in 1920, reported a case of infection of the mouth caused by Monilia candida. Castellani,[2] in 1925, noted a swelling of the tongue due to a yeastlike organism, Cryptococcus macroglossiae. Zeisler,[3] in 1927, found infections of the tongue in two cases; one caused by Monilia pinioyi was associated with a polycythemia vera and chronic arteriosclerotic myocarditis. In this case the tongue was covered with exanthemic white streaks. The second case was that of a mycosis of the lips and tongue, producing a macrocheilia and a macroglossia. The tongue was covered with lateral fissures and grayish translucent streaks. The organism isolated was a Cryptococcus. Frost,[4] in 1929, reported a case due to Monilia pinioyi, which was associated with a lesion on the skin.

## REPORT OF A CASE

*History.*—G. P. McI., a white man, aged 24, had a coated tongue. This condition had persisted and had become worse during the twelve months prior to examination. The entire dorsal surface of the tongue was covered with a heavy, thick, white deposit which necessitated mechanical removal several times a day. The growth increased in height from the tip backward. He had chronic constipation associated with attacks of indigestion. On several occasions small amounts

From the Department of Bacteriology, University of Washington, and the Policlinic.

1. Engman, M.D., and Weiss, R. S.: Monilia Candida of Mouth, Arch. Dermat. & Syph. **1**:119 (Feb.) 1920.

2. Castellani, Aldo: Notes on Three New Yeast-Like Organisms and a New Bacillus, with Remarks on the Clinical Conditions from Which They Have Been Isolated, J. Trop. Med. **28**:217, 1925.

3. Zeisler, E. P.: Monilia Infection of the Tongue, Arch. Dermat. & Syph. **15**:171 (Feb.) 1927.

4. Frost, K.; Sutherland-Campbell, H., and Plunkett, O. A.: Monilia of Tongue: Report of Instance with Associated Skin Lesions, Arch. Dermat. & Syph. **20**:811 (Dec.) 1929.

of bright blood were noticed on the feces. No mucus was found. There had been a loss of 30 pounds (13.6 Kg.) in weight during the last two years. The physical condition had been good until two years previous to examination, when the loss in weight began. At that time constipation became aggravated, and the patient was troubled with "gas on his stomach" and nervousness. Because of this condition he underwent a tonsillectomy, but there was no improvement. One year later gingivitis developed associated with a coated tongue, which was diagnosed as Vincent's angina. Treatment directed toward the eradication of this condition was without effect.

*Physical Examination.*—The patient was a fairly well nourished man, weighing 135 pounds (61.2 Kg.). The cardiovascular, renal and pulmonary systems were normal. The sinuses were clear, and the teeth were in a good state. Laboratory reports were negative, except for a growth on the tongue. Gastro-intestinal examination revealed a moderately atonic, slowly emptying stomach associated with marked ptosis of the transverse colon and a moderate degree of spasticity of the

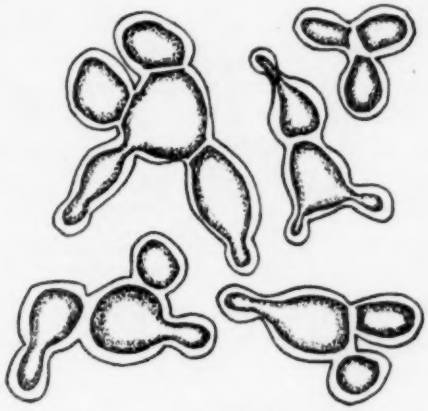

Fig. 1.—Yeast form of Monilia bronchialis; × 2,200.

left transverse and descending parts of the colon. Rectal examination gave negative results.

*Strain of Monilia Isolated.*—Scrapings from the tongue of the patient revealed yeastlike organisms and mycelial threads accompanied by saprophytic streptococci. For isolation of the organism, the scrapings were placed in a deep dextrose broth tube and then plated on dextrose agar. For purposes of identification the organism was grown on maltose agar (Sabouraud's medium), dextrose agar, litmus lactose agar, gelatin, litmus milk, 1 per cent dextrose, maltose, sucrose, lactose, levulose, salicin, mannite, arabinose, dulcit and galactose broths.

Morphology: At the end of twenty-four hours a slide made from a dextrose agar culture showed a large, oval, nonvacuolated, yeastlike organism (4 by 7 microns) (fig. 1). The cell wall was very thin. The nucleus was not easily distinguished at any time. After seven days the yeast cells still predominated in the medium. Although there was a slight tendency to the production of mycelial threads of from 2 to 4 cells in length, there was practically no vacuolation in the yeast cells.

On gelatin only yeast cells persisted after three weeks.

On maltose and lactose litmus agar the morphology was the same as that found on dextrose agar. However, on plain agar, on which the growth was very sparse, a long segmented mycelium was observed after two days. It was on this medium that the greatest tendency to sporulation was seen (fig. 2).

In dextrose broth at the end of twenty-four hours the yeast showed a solid-staining, almost oval cell with prolific budding. The bud was characteristically attached to the mother cell by a very fine thread of protoplasm. In all the broth cultures after seven days there was a distinct tendency toward the formation of mycelium. Capsules were not found on any medium.

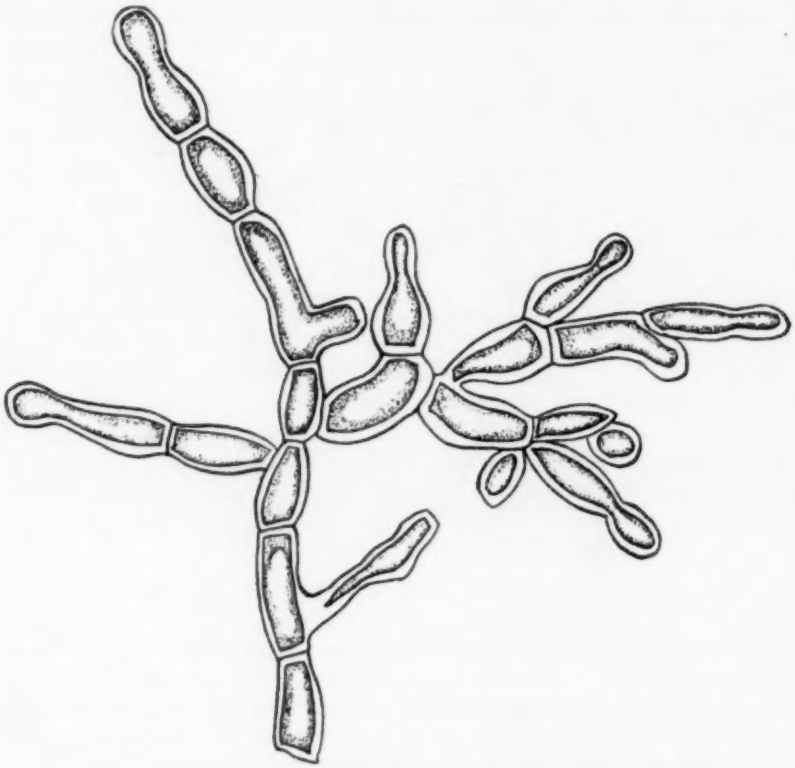

Fig. 2.—Mycelium and spores of Monilia bronchialis; × 2,200.

Reproduction: Four forms of reproduction were observed. The simple yeast-like form reproduced by budding. At no time were ascospores observed. The mycelial threads reproduced in three ways, namely, by chlamydospores, by terminal clusters of conidial spores from eight to twelve in number and by lateral or terminal single spores. After one week in dextrose broth the latter showed a dark brownish wall, which gave the white culture a brownish-gray appearance. This seemed to be a resting stage; with the formation of such a type of sporulation, the mycelial threads were entirely emptied of protoplasm. The germination of the spores was lateral.

Staining Reactions: Both the yeastlike and the mycelial forms stained readily with all aniline stains and were gram-positive, but they were not acid-fast.

Cultural Characteristics: On dextrose agar and maltose agar slants, incubated at 37 C., the colony was creamy white, luxuriant and elevated, with a regular edge. On litmus lactose agar and plain agar the growth was sparse and regular. There was no change in the litmus lactose agar. On a dextrose agar plate it produced a characteristic triangular colony, elevated in the center.

On gelatin it grew along the line of puncture in a fine unspreading form. It did not liquefy gelatin.

It was inert in milk. There was a tendency toward the formation of a heavy sediment but a slight tendency toward collar formation. It fermented only with acid and gas dextrose, maltose and sucrose.

These observations agree with the description of Monilia bronchialis Castellani,[5] with the exception that the organism obtained in this case did not ferment levulose.

## ANIMAL EXPERIMENTATION

The pathogenicity of this organism was tested by inoculation into three animals: a rabbit weighing 2,000 Gm., a guinea-pig weighing 700 Gm. and a white rat weighing 100 Gm. The rabbit was given 5 cc. of a twenty-four hour dextrose broth culture intravenously, and 2 cc. of the same culture was administered intraperitoneally to the rat. The guinea-pig was given 2 cc. of a broth culture at two-day intervals over a period of six days. After seven days none of the animals showed any symptoms, with the exception of the guinea-pig, in which a small abscess was formed at the point of inoculation. All of the animals were killed after one week. No gross lesions were found in any of them. The organism was recovered, however, from the heart's blood and the peritoneal fluid of the rat and from the abscess and peritoneal fluid of the guinea-pig.

## SUMMARY

An organism which was apparently an atypical strain of Monilia bronchialis described by Castellani was isolated from the patient's tongue. It differed from the strain described by him only in the fact that it did not ferment levulose. The only pathologic change produced on inoculation into a guinea-pig was an abscess at the point of inoculation.

5. Castellani, Aldo: Blastomycosis and Some Other Conditions Due to Yeast-Like Fungi, Am. J. Trop. Med. **8**:379 (Sept.) 1928.

# EXFOLIATIVE DERMATITIS FROM BUTESIN PICRATE OINTMENT

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Every dermatologist has seen cases of dermatitis due to the application of butesin picrate ointment and from solutions of picric acid, and cases have been reported by Pusey [1] and Jackson.[2]

In the case herein reported, a generalized exfoliative dermatitis developed following the local application of butesin picrate ointment to abrasions of the leg.

Butesin picrate is not a mixture of butesin and picric acid, but is a chemical combination (dinormalbutyl-*p*-aminobenzoate trinitrophenol) containing 63 per cent butesin and 37 per cent trinitrophenol (picric acid).

## REPORT OF A CASE

H. M., a white man, a laborer, aged 41, first seen on July 24, 1930, presented a generalized exfoliative dermatitis. He stated that six weeks previously he had received several abrasions on the left leg, which had become infected. The industrial physician used several ointments and finally applied butesin picrate ointment. There were burning and itching during the night, and on the following morning when the bandage was removed the leg was erythematous. During the next few days the skin over the body became inflamed and scaly. The generalized eruption increased, and the patient applied for treatment at the hospital.

The exfoliative dermatitis improved in a reasonable length of time when soothing applications and emollients were used. When the appearance of the skin was again normal, patch tests were made with the following substances: mercuric chloride 1:1,000, ammoniated mercuric ointment 5 per cent, hydrous wool fat, U. S. P., resorcinol monoacetate ointment 5 per cent, iodex ointment, mercurochrome-220 soluble 2 per cent, petrolatum and butesin picrate ointment. Readings were made in twenty-four hours, and there was a definite erythema at the site of

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1. Pusey, W. A., and Rattner, H.: Dermatitis from Butesin Picrate, Arch. Dermat. & Syph. **19**:917 (June) 1929.

2. Jackson, N. R.: Dermatitis from Picric Acid Solution and Butesin Picrate Ointment, Arch. Dermat. & Syph. **21**:40 (Jan.) 1930.

the application of the butesin picrate ointment; all other areas were normal. At the end of forty-eight hours the erythema had increased; the area was edematous, and several vesicles the size of a pinhead were present. Control tests made on other persons gave negative results.

### COMMENT

This case is reported because of its unusual character and because no cases of generalized eruption due to the local use of butesin picrate ointment have been reported.

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# THE TREATMENT FOR LICHEN PLANUS WITH INTRAMUSCULAR INJECTIONS OF BISMUTH SALICYLATE IN OIL

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At times lichen planus does not respond readily to the usual methods of treatment, such as intramuscular injections of mercury or arsenic, roentgen exposures or any combination of these. Therefore, any method that might be used as an adjuvant to present methods of treatment or any new method that does as well or better than the present known ones is worth adding to the armamentarium. Bismuth salicylate, when injected intramuscularly, is such a drug, and is worth trying either at the onset of treatment or after other methods have failed.

In a series of fifteen cases in which the patients were treated over a period of three years, fourteen took the prescribed course of treatment and are well; one took only a partial course and was improved when last seen. The full course of treatment consists of 1½ grains (0.1 Gm.) of bismuth salicylate intramuscularly once a week for from ten to twelve treatments. Frequently, fewer injections are needed. Bismuth salicylate in olive oil is the type of drug used.

The following typical case histories will demonstrate the response of this disease to injections of bismuth:

## REPORT OF CASES

CASE 1.—H. K., a man, aged 72, had lichen planus of one month's duration. There was a moderate typical eruption over the legs and buttocks, with slight itching. He was given injections of bismuth salicylate on Dec. 6 and Dec. 13, 1929. By the end of the second week the lesions had flattened out and were replaced by brown pigment. Itching disappeared after the first injection. There was no recurrence when the patient was last seen, on Feb. 7, 1930.

CASE 2.—J. C., a man, aged 45, had about a half dozen annular groups of lesions on each leg. There was much itching, and the disease had been present for one year. Four injections of bismuth salicylate were given at weekly intervals from Jan. 17 to Feb. 7, 1930. At the end of this time the lesions had disappeared and were replaced by brown pigment. The patient was last seen on May 18, and the pigment was fading. There were no new lesions, and the patient was perfectly comfortable.

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CASE 3.—F. G., a woman, aged 47, had generalized lichen planus accompanied by very severe itching, which had occurred two months prior to admission. She was given calamine lotion locally to help relieve the itching. She received twelve injections of bismuth salicylate at weekly intervals between March 6 and May 6, 1930. The itching did not subside altogether until after she had received six treatments. During the first five weeks of treatment, new papules developed while others were receding. After six weeks all of the lesions had gradually flattened out and were replaced by brownish pigmentation. When seen on July 28, there was still pigmentation, but no new lesions had developed and the patient was quite comfortable.

CASE 4.—A. B., a woman, aged 44, had had recurring lesions over her arms, forearms, hands and legs for twenty years. The itching at times was almost unbearable. She had had all types of treatment, including injections of arsenic and mercury and roentgen exposures. After seven injections of bismuth salicylate at approximately weekly intervals, the lesions flattened out considerably and the itching practically disappeared. The patient did not return for further treatment, but was definitely improved at the time.

CASE 5.—H. W., a woman, aged 60, had lichen planus hypertrophicus of one year's duration, which was present on the anterior surface of the legs and thighs. There was much itching. Calamine lotion was used locally, and she was given ten injections of bismuth salicylate at weekly intervals; the lesions flattened considerably. The skin was definitely less horny, and the subjective symptoms disappeared. The patient had had other types of treatment prior to admission to the clinic, and she said that she felt better after these injections than at any other time during the course of the disease. The eruption had not completely disappeared before it was necessary for the patient to leave town, so no record as to the ultimate result is available.

Of course, in giving bismuth salicylate one must watch the gum line for signs of intolerance, and at the first sign of bismuth poisoning treatment must be stopped. To date, there has been no trouble with the use of this drug in any of the fifteen cases.

Dr. Radnai[1] of Budapest was the first to report on the use of bismuth salicylate in the treatment for lichen planus. He had good success with its use, but his technic was a bit different from mine. He used 1½ grains (0.1 Gm.) per injection and gave from two to three treatments per week for a course of twenty injections.

## CONCLUSIONS

In a series of fifteen cases of lichen planus, intramuscular injections of bismuth salicylate in doses of 1½ grains (0.1 Gm.) once weekly for about ten treatments have effected cures in fourteen cases and improvement in one other. Bismuth salicylate is an agent worth trying in this condition.

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1. Radnai, Ernst: Die Heilung des Lichen ruber planus mit Bismut-Injektionen, Monatschr. ungar. Med. **1**:209 (Dec.) 1927.

# CHOLESTEROL AND LECITHIN STUDIES OF SKIN DISEASES

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This paper deals with the investigation of the cholesterol and lecithin content of whole blood in a miscellaneous group of skin diseases: acne vulgaris, alopecia areata, alopecia cicatrizata, Bazin's disease, chloasma, neurodermatitis, occupational dermatitis, seborrheic dermatitis, dermatitis venenata, dermatophytosis with general and localized involvements, chronic eczema, furunculosis, herpes zoster, keloid, lichen planus, lipoma, lupus erythematosus, onychomycosis of the hands, pityriasis rosea, prurigo nodularis, psoriasis, purpura simplex, sarcoid, tinea capitis and versicolor, urticaria, von Recklinghausen's disease and xanthoma. Our object in undertaking this work was primarily to ascertain whether there are variations in the blood lipids in these diseases. An accumulation of such data may be helpful in discovering the still doubtful etiology of certain of these dermatoses, in alleviating the symptoms and, perhaps, in finally attaining proper therapeusis. This is an immense program. Hence, the study to be detailed presently cannot be considered more than an introduction although several interesting results have been obtained.

The choice of subjects and the methods for analysis were the same as those described in our previous work.[1]

In this, our eleventh study of cholesterol and lecithin, it is perhaps opportune to note how well our results may be duplicated. In table 1 is a series of cholesterol and lecithin determinations on whole blood from patients affected with acne vulgaris.

A glance at these figures reveals the close reproducibility of results. Moreover, practically the same distribution of values was obtained for two series of cases of dermatophytosis (tables 2 and 3).

Incidentally, this does not mean that the cholesterol and lecithin content of whole blood is always exactly the same. Analyses for these substances in blood from the same persons at intervals varying from several days to several weeks yielded the results given in table 4.

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From the Department of Dermatology and Syphilology, Post-Graduate Medical School and Hospital, Columbia University.

1. Rosen, Isadore, and Krasnow, Frances: Lecithin and Cholesterol Studies in Dermatophytosis, Arch. Dermat. & Syph. **23**:132 (Jan.) 1931.

To economize on space, the detailed protocols of the 360 cases studied have been omitted. Instead, summaries are given that outline the results obtained. The diseases are listed in alphabetical order. Table 5 shows that the average values for cholesterol ranged from 158 ± 14 in forty-four cases of acne vulgaris (the average for two cases of alopecia areata was 149 ± 14) to 232 ± 153 mg. per hundred cubic centimeters of whole blood in six cases of xanthoma. For lecithin the series includes

TABLE 1.—*Cholesterol and Lecithin Determinations in Acne Vulgaris*

| | Mg. per 100 Cc. of Whole Blood | | | | | | | | | |
|---|---|---|---|---|---|---|---|---|---|---|
| Cholesterol | | | | | | | | | | |
| Before roentgen treatment | 140 | 166 | 166 | 167 | 169 | 178 | 189 | 193 | 203 | 204 |
| Immediately after roentgen treatment | 138 | 166 | 166 | 166 | 172 | 176 | 193 | 202 | 197 | 202 |
| Lecithin | | | | | | | | | | |
| Before roentgen treatment | 242 | 255 | 252 | 255 | 242 | 257 | 232 | 262 | 260 | 267 |
| After roentgen treatment | 232 | 255 | 255 | 245 | 237 | 260 | 225 | 262 | 260 | 265 |

TABLE 2.—*Cholesterol Values in Dermatophytosis*

| | Mg. per 100 Cc. of Whole Blood | Number of Cases | | Percentage of Total | |
|---|---|---|---|---|---|
| | | 1930 | 1931 | 1930 | 1931 |
| Total | ..... | 80 | 80 | | |
| Below range | 171 — 16 | 16 | 12 | 20 | 15 |
| Within range | 171 ± 16 | 42 | 45 | 53 | 56 |
| Above range | 171 + 16 | 20 | 23 | 25 | 29 |

TABLE 3.—*Lecithin Values in Dermatophytosis*

| | Mg. per 100 Cc. of Whole Blood | Number of Cases | | Percentage of Total | |
|---|---|---|---|---|---|
| | | 1930 | 1931 | 1930 | 1931 |
| Total | ..... | 61 | 80 | | |
| Below range | 242 — 22 | 0 | 4 | 0 | 5 |
| Within range | 242 ± 22 | 37 | 45 | 60 | 56 |
| Above range | 242 + 22 | 24 | 31 | 40 | 39 |

TABLE 4.—*Cholesterol and Lecithin Content of Whole Blood*

| | Date | Cholesterol, Mg. per 100 Cc. of Whole Blood | Lecithin, Mg. per 100 Cc. of Whole Blood |
|---|---|---|---|
| Acne | 12/26/30 | 166 | 272 |
| | 12/29/30 | 177 | 282 |
| | 10/15/30 | 171 | 245 |
| | 12/15/30 | 173 | 252 |
| Pityriasis rosea | 10/ 8/30 | 224 | 242 |
| | 1/16/31 | 202 | 300 |
| | 1/13/31 | 283 | 317 |
| | 1/20/31 | 275 | 312 |

TABLE 5.—*Summary of the Cholesterol and Lecithin Content of Whole Blood in Thirty-Two Different Skin Diseases*

| Description of Cases | Number of Cases | Average Cholesterol, Mg. per 100 Cc. | Average Lecithin, Mg. per 100 Cc. |
|---|---|---|---|
| Normal | 27 | 171 ± 16 | 242 ± 22 |
| Acne vulgaris | 44 | 158 ± 14 | 244 ± 13 |
| Alopecia areata | 2 | 149 ± 14 | 267 ± 15 |
| Alopecia cicatrizata | 2 | 171 ± 13 | 255 ± 5 |
| Bazin's disease | 2 | 173 ± 4 | 251 ± 1 |
| Chloasma | 1 | 190 | 285 |
| Dermatitis, neuro- | 6 | 184 ± 18 | 269 ± 17 |
| Dermatitis, occupational | 4 | 168 ± 11 | 245 ± 15 |
| Dermatitis, seborrheic | 3 | 177 ± 8 | 270 ± 16 |
| Dermatitis, venenata | 9 | 179 ± 20 | 279 ± 21 |
| Dermatophytosis | | | |
| with dermatophytids | 49 | 176 ± 13 | 259 ± 18 |
| on feet only | 21 | 178 ± 19 | 259 ± 21 |
| on trunk only | 10 | 174 ± 24 | 258 ± 16 |
| Total | 80 | 176 ± 16 | 259 ± 18 |
| Eczema, chronic | 5 | 171 ± 13 | 257 ± 19 |
| Furunculosis | 3 | 157 ± 14 | 246 ± 12 |
| Herpes zoster | 3 | 193 ± 19 | 260 ± 28 |
| Keloid | 3 | 182 ± 28 | 266 ± 4 |
| Lichen planus | 5 | 184 ± 13 | 259 ± 17 |
| Lipoma | 5 | 212 ± 37 | 265 ± 18 |
| Lupus erythematosus | 6 | 173 ± 20 | 249 ± 16 |
| Onychomycosis of hands | 10 | 199 ± 27 | 278 ± 19 |
| Pityriasis rosea | 11 | 183 ± 31 | 251 ± 16 |
| Prurigo nodularis | 1 | 154 | 272 |
| Psoriasis | 35 | 165 ± 13 | 248 ± 16 |
| Psoriasis and dermatophytosis | 7 | 177 ± 20 | 271 ± 13 |
| Purpura simplex | 2 | 176 ± 18 | 261 ± 1 |
| Sarcoid | 1 | 203 | 295 |
| Tinea capitis | 9 | 172 ± 20 | 263 ± 10 |
| Tinea versicolor | 3 | 210 ± 16 | 275 ± 9 |
| Urticaria | 4 | 187 ± 22 | 260 ± 17 |
| Urticaria pigmentosa | 2 | 191 ± 5 | 254 ± 5 |
| von Recklinghausen's disease | 2 | 259 ± 45 | 261 ± 24 |
| Xanthoma | 6 | 232 ± 153 | 286 ± 60 |

TABLE 6.—*Percentage of Cases Showing Different Levels of Cholesterol in Whole Blood*

| Description of Cases | Number of Cases | Percentage of Cases Showing Cholesterol Content of Whole Blood | | |
|---|---|---|---|---|
| | | Below 171 − 16 Mg. per 100 Cc. | Within 171 ± 16 Mg. per 100 Cc. | Above 171 + 16 Mg. per 100 Cc. |
| Normal | 99 | 16 | 68 | 16 |
| Acne vulgaris | 44 | 23 | 66 | 11 |
| Alopecia areata | 2 | 50 | 50 | 0 |
| Alopecia cicatrizata | 2 | 0 | 100 | 0 |
| Bazin's disease | 2 | 0 | 100 | 0 |
| Chloasma | 1 | 0 | 0 | 100 |
| Dermatitis, neuro- | 6 | 0 | 67 | 33 |
| Dermatitis, occupational | 4 | 25 | 75 | 0 |
| Dermatitis, seborrheic | 3 | 0 | 100 | 0 |
| Dermatitis, venenata | 9 | 11 | 56 | 33 |
| Dermatophytosis | | | | |
| with dermatophytids | 49 | 10 | 63 | 27 |
| on feet only | 21 | 19 | 47 | 33 |
| on trunk only | 10 | 30 | 40 | 30 |
| Total | 80 | 15 | 56 | 29 |
| Eczema, chronic | 5 | 20 | 60 | 20 |
| Furunculosis | 3 | 33 | 67 | 0 |
| Herpes zoster | 3 | 0 | 33 | 67 |
| Keloid | 3 | 33 | 33 | 33 |
| Lichen planus | 5 | 0 | 40 | 60 |
| Lipoma | 5 | 20 | 20 | 60 |
| Lupus erythematosus | 6 | 33 | 33 | 33 |
| Onychomycosis of hands | 10 | 10 | 20 | 70 |
| Pityriasis rosea | 11 | 36 | 27 | 36 |
| Prurigo nodularis | 1 | 100 | 0 | 0 |
| Psoriasis | 35 | 29 | 63 | 9 |
| Psoriasis and dermatophytosis | 7 | 0 | 28 | 71 |
| Purpura simplex | 2 | 0 | 50 | 50 |
| Sarcoid | 1 | 0 | 0 | 100 |
| Tinea capitis | 9 | 33 | 33 | 33 |
| Tinea versicolor | 3 | 0 | 33 | 67 |
| Urticaria | 4 | 0 | 75 | 25 |
| Urticaria pigmentosa | 2 | 0 | 50 | 50 |
| von Recklinghausen's disease | 2 | 0 | 100 | 0 |
| Xanthoma | 6 | 0 | 17 | 83 |

figures from 244 ± 13 for the acne group to 286 ± 60 mg. per hundred cubic centimeters of whole blood for the patients with xanthoma (one case of sarcoid showed 295 mg. per hundred cubic centimeters of whole blood).

TABLE 7.—*Percentage of Cases Showing Different Levels of Lecithin in Whole Blood*

| Description of Cases | Number of Cases | Percentage of Cases Showing Lecithin Content of Whole Blood | | |
|---|---|---|---|---|
| | | Below 242 − 22 Mg. per 100 Cc. | Within 242 ± 22 Mg. per 100 Cc. | Above 242 + 22 Mg. per 100 Cc. |
| Normal | 27 | 7 | 78 | 14 |
| Acne vulgaris | 44 | 2 | 86 | 11 |
| Alopecia areata | 2 | 0 | 50 | 50 |
| Alopecia cicatrizata | 2 | 0 | 100 | 0 |
| Bazin's disease | 2 | 0 | 100 | 0 |
| Chloasma | 1 | 0 | 0 | 100 |
| Dermatitis, neuro- | 6 | 0 | 33 | 67 |
| Dermatitis, occupational | 4 | 0 | 75 | 25 |
| Dermatitis, seborrheic | 3 | 0 | 33 | 67 |
| Dermatitis, venenata | 9 | 0 | 22 | 78 |
| Dermatophytosis | | | | |
| with dermatophytids | 49 | 6 | 57 | 37 |
| on feet only | 21 | 5 | 47 | 47 |
| on trunk only | 10 | 0 | 70 | 30 |
| Total | 80 | 5 | 56 | 38 |
| Eczema, chronic | 5 | 0 | 60 | 40 |
| Furunculosis | 3 | 0 | 67 | 33 |
| Herpes zoster | 3 | 33 | 0 | 67 |
| Keloid | 3 | 0 | 33 | 67 |
| Lichen planus | 5 | 0 | 60 | 40 |
| Lipoma | 5 | 0 | 40 | 60 |
| Lupus erythematosus | 6 | 0 | 67 | 33 |
| Onychomycosis of hands | 10 | 10 | 20 | 70 |
| Pityriasis rosea | 11 | 0 | 82 | 18 |
| Prurigo nodularis | 1 | 0 | 0 | 100 |
| Psoriasis | 35 | 9 | 66 | 25 |
| Psoriasis and dermatophytosis | 7 | 0 | 42 | 57 |
| Purpura simplex | 2 | 0 | 100 | 0 |
| Sarcoid | 1 | 0 | 0 | 100 |
| Tinea capitis | 9 | 0 | 56 | 44 |
| Tinea versicolor | 3 | 0 | 33 | 67 |
| Urticaria | 4 | 0 | 75 | 25 |
| Urticaria pigmentosa | 2 | 0 | 100 | 0 |
| von Recklinghausen's disease | 2 | 0 | 50 | 50 |
| Xanthoma | 6 | 17 | 17 | 67 |

TABLE 8.—*Data for Chart 1 (Curves I, II, III, IIIa, IV): Cholesterol Values for Normal Subjects and Patients Suffering from Various Skin Diseases*

| I Normal (99 Cases) | | | II Acne (44 Cases) | | | III Dermatophytosis with Dermatophytids (49 Cases) | | | IIIa Dermatophytosis with Various Degrees of Involvement (80 Cases) | | | IV Psoriasis (35 Cases) | | |
|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|
| Mg. | No. | % | Mg. | No. | % | Mg. | No. | % | Mg. | No. | % | Mg. | No. | % |
| 140-9 | 5 | 5.2 | 120-9 | 1 | 2.3 | 130-9 | 1 | 2.0 | 130-9 | 3 | 3.8 | 130-9 | 1 | 2.7 |
| 150-9 | 21 | 21.2 | 130-9 | 1 | 2.3 | 140-9 | 2 | 4.0 | 140-9 | 6 | 7.5 | 140-9 | 5 | 14.2 |
| 160-9 | 29 | 29.3 | 140-9 | 4 | 9.1 | 150-9 | 5 | 10.0 | 150-9 | 7 | 8.8 | 150-9 | 8 | 22.8 |
| 170-9 | 16 | 16.2 | 150-9 | 8 | 18.2 | 160-9 | 10 | 20.0 | 160-9 | 15 | 18.7 | 160-9 | 10 | 28.6 |
| 180-9 | 12 | 12.2 | 160-9 | 16 | 36.4 | 170-9 | 13 | 25.0 | 170-9 | 15 | 18.7 | 170-9 | 5 | 14.2 |
| 190-9 | 7 | 7.3 | 170-9 | 5 | 11.3 | 180-9 | 6 | 12.0 | 180-9 | 13 | 16.2 | 180-9 | 3 | 8.6 |
| 200-9 | 8 | 8.2 | 180-9 | 5 | 11.3 | 190-9 | 6 | 12.0 | 190-9 | 9 | 11.2 | 190-9 | 2 | 5.7 |
| 210-9 | 1 | 1.2 | 190-9 | 2 | 4.5 | 200-9 | 5 | 10.0 | 200-9 | 7 | 8.8 | 200-9 | 1 | 2.7 |
| | | | 200-9 | 2 | 4.5 | 210-9 | 1 | 2.0 | 210-9 | 4 | 5.0 | | | |
| | | | | | | | | | 220-9 | 1 | 1.3 | | | |

In table 6 is presented the percentage of cases in each disease, giving cholesterol values below the low normal figure, within the normal range or above the high normal figure. In seven instances the values were above the high normal average of 171 + 16 mg. per hundred cubic centimeters of whole blood, and in twenty-five instances they were above the normal mean of 171 mg. per hundred cubic centimeters of whole blood. On the other hand, the number of instances in which the cholesterol values fell below the low normal average or below the mean were very few, being one and three, respectively. This same tendency may be observed in the figures for the lecithin content in table 7. Here ten instances showed lecithin values above the high normal average of

TABLE 9.—*Data for Chart 2 (Curves V, VI, VII, VIIa, VIII): Lecithin Values for Normal Persons and Patients Suffering from Various Skin Diseases*

| V Normal (27 Cases) | | | VI Acne (44 Cases) | | | VII Dermatophytosis with Dermatophytids (49 Cases) | | | VIIa Dermatophytosis with Various Degrees of Involvement (80 Cases) | | | VIII Psoriasis (35 Cases) | | |
|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|
| Mg. | No. | % | Mg. | No. | % | Mg. | No. | % | Mg. | No. | % | Mg. | No. | % |
| 170-9 | 1 | | 210-9 | 1 | 2.3 | 200-9 | 1 | 6.1 | 200-9 | 1 | 5.0 | 200-9 | 0 | 8.6 |
| 180-9 | 0 | | 220-9 | 3 | 27.3 | 210-9 | 2 | | 210-9 | 3 | | 210-9 | 3 | |
| 190-9 | 1 | 7.4 | 230-9 | 9 | | 220-9 | 1 | 8.2 | 220-9 | 4 | 13.7 | 220-9 | 3 | 25.7 |
| 200-9 | 0 | | 240-9 | 9 | 47.6 | 230-9 | 4 | | 230-9 | 7 | | 230-9 | 6 | |
| 210-9 | 0 | | 250-9 | 12 | | 240-9 | 12 | 42.9 | 240-9 | 15 | 33.7 | 240-9 | 5 | 31.4 |
| 220-9 | 4 | 33.0 | 260-9 | 8 | 27.3 | 250-9 | 9 | | 250-9 | 12 | | 250-9 | 6 | |
| 230-9 | 5 | | 270-9 | 4 | | 260-9 | 6 | 28.6 | 260-9 | 13 | 30.0 | 260-9 | 6 | 26.6 |
| 240-9 | 5 | 37.0 | 280-9 | 1 | 2.3 | 270-9 | 8 | | 270-9 | 11 | | 270-9 | 4 | |
| 250-9 | 5 | | 290-9 | 0 | | 280-9 | 4 | 10.0 | 280-9 | 6 | 12.5 | 280-9 | 2 | 5.7 |
| 260-9 | 2 | 22.2 | | | | 290-9 | 1 | | 290-9 | 4 | | | | |
| 270-9 | 4 | | | | | 300-9 | 2 | 4.1 | 300-9 | 2 | 5.0 | | | |
| | | | | | | | | | 310-9 | 2 | | | | |

242 + 22 mg. per hundred cubic centimeters of whole blood and thirty instances values above the mean, 242 mg., whereas there were no averages below the low normal and no values below the mean. In general, therefore, the cholesterol and lecithin content of whole blood tends toward high values. However, the former is more often low than the latter. That cholesterol fluctuates more than lecithin is likewise discernible from the frequency curves in charts 1 and 2. The peaks on the cholesterol curves are not quite so steep as those on the lecithin curves. Moreover, whereas all the lecithin curves have their peaks in the same range, the cholesterol curves are not so characterized.

It is interesting to note that of the five sets of curves that for psoriasis (curves IV and VIII) approaches the normal most closely.

The high peaks in the acne curves (II and VI) are striking, showing the tendency for both cholesterol and lecithin in this disease to attain the normal value. Our aim was to obtain curves for the entire list of dermatoses, but too few cases have yet been studied to enable us to plot a sufficient number of points for continuous curves.

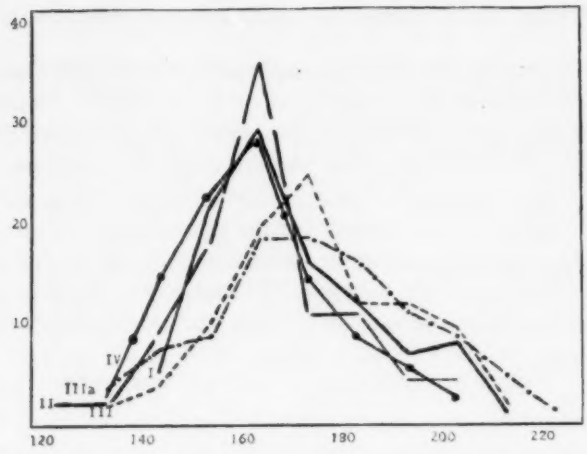


Chart 1.—Curves showing the frequency of occurrence of cholesterol values in patients suffering from acne, dermatophytosis and psoriasis as compared with that in normal subjects. The vertical scale represents the percentage of cases and the horizontal scale the number of milligrams of cholesterol per hundred cubic centimeters of whole blood. *I*, normal state; *II*, acne; *III*, dermatophytosis with dermatophytids; *IIIa*, dermatophytosis with various degrees of involvement; *IV*, psoriasis.

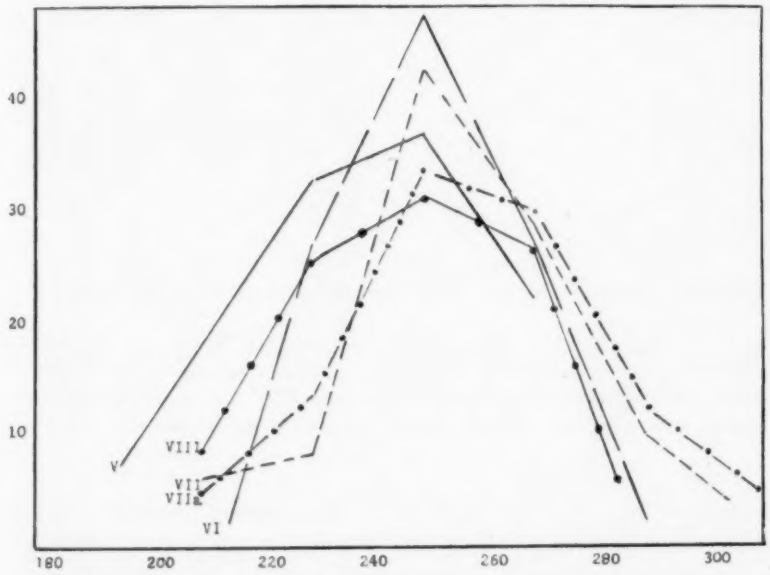


Chart 2.—Curves showing the frequency of occurrence of lecithin values in patients suffering from acne, dermatophytosis and psoriasis as compared with that in normal subjects. The vertical scale represents the percentage of cases and the horizontal scale the number of milligrams of lecithin per hundred cubic centimeters of whole blood. *V*, normal state; *VI*, acne; *VII*, dermatophytosis with dermatophytids; *VIIa*, dermatophytosis with various degrees of involvement; *VIII*, psoriasis.

Although not apparent from the tables, a certain degree of proportionality exists between the cholesterol and the lecithin values. Evidence may be obtained by observing the scatter of points represented on a graph, with the lecithin values plotted along the abscissa and the cholesterol values along the ordinate. This was done for acne, dermatophytosis and psoriasis. The graph for dermatophytosis, chart 3, shows a considerable degree of correlation, which is indicated by the comparative absence of points in the upper left and lower right areas. (If cholesterol and lecithin were exactly proportional, the points would be

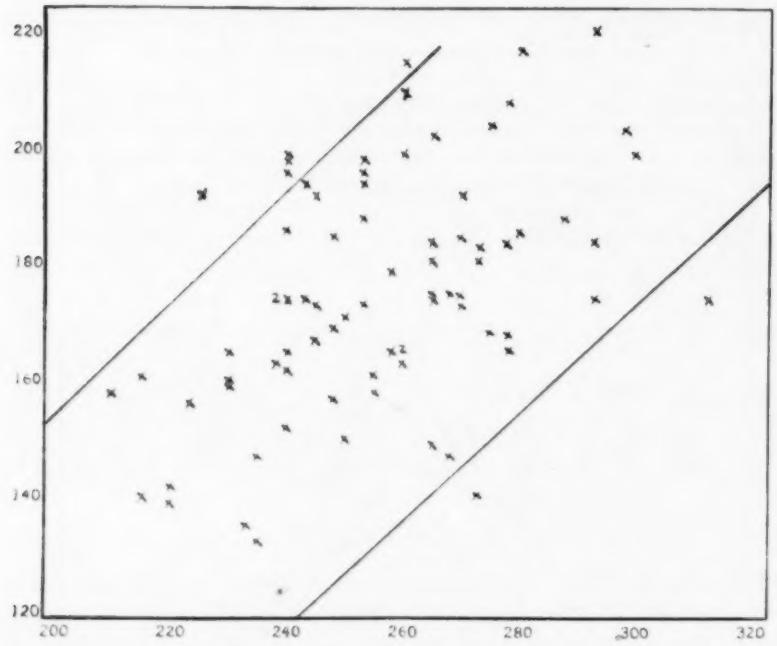


Chart 3.—Graph showing the proportionality between lecithin and cholesterol in dermatophytosis. The vertical scale represents the number of milligrams of cholesterol per hundred cubic centimeters of whole blood and the horizontal scale the number of milligrams of lecithin per hundred cubic centimeters of whole blood.

on a straight line.) The other conditions present similar pictures, though not as marked. We did not attempt to make graphs for the other twenty-nine diseases because the number of cases thus far assembled were too few.

## CONCLUSIONS

In conclusion, then, we have demonstrated:

1. Our technic is accurately reproducible.

2. In general, the cholesterol content of whole blood tends to be high in dermatoses. Twenty per cent of the averages were above the high normal of 171 + 16 mg. per hundred cubic centimeters of whole blood, and only 3 per cent fell below the low normal, 171 — 16 mg. per hundred cubic centimeters of whole blood. The lowest averages obtained were those for acne, alopecia areata and furunculosis; the highest, those for neurodermatitis, lipoma, onychomycosis, von Recklinghausen's disease and xanthoma. Again, 78 per cent of the mean values were above the normal mean, while only 9 per cent were less than the normal mean.

3. In general, the lecithin content of whole blood in dermatoses tends to be high. Forty-one per cent of the averages were above the high normal, 242 + 22 per hundred cubic centimeters, and none below the low normal, 242 — 22 mg. The lowest averages were those for acne, occupational dermatitis, furunculosis and psoriasis. The highest averages obtained were those for dermatitis venenata, onychomycosis and von Recklinghausen's disease. Of the means, 93 per cent were above the normal and none below.

4. A certain degree of proportionality exists between the cholesterol and the lecithin content of whole blood in the dermatoses studied.

# GENERALIZED TELANGIECTASIA AND SINUS INFECTION

## REPORT OF A CASE WITH CURE BY TREATMENT OF CHRONIC SINUSITIS

SAMUEL AYRES, JR., M.D.

LLOYD A. BURROWS, M.D.

AND

NELSON PAUL ANDERSON, M.D.

LOS ANGELES

Generalized telangiectasia is one of the rarer dermatoses, and little is known concerning its etiology and treatment. Becker [1] reviewed the literature thoroughly, and to the fifty-four cases already recorded added four cases of generalized telangiectasia without involvement of the mucous membranes which were seen at the Mayo Clinic.

For purposes of classification this entity is to be distinguished from livedo racemosa, cutis marmorata and purpura annularis telangiectoides (Majocchi), although all four conditions may be closely related etiologically.

The appearance in generalized telangiectasia consists of a more or less diffuse redness covering all or large portions of the cutaneous surface, with a vague capillary network from which the color can be pressed. At times the redness appears to be accentuated in a punctiform manner; at other times the reticulated capillaries seem to form indistinct rings of from 1 to 2 cm. in diameter. Becker noticed petechiae in one of his cases, and in another the lesions occurred on the upper part of the arms as six erythematous plaques, ranging in size up to 5 by 10 cm., with ill defined borders. The patients may complain of burning and itching.

Sixteen of the fifty-four cases reviewed by Becker were regarded as syphilitic, thirteen cases had evidence of cardiac or renal impairment, twenty-six showed endocrine disturbances, which included puberty and obesity, while twelve cases showed either urticaria or dermographism. Focal infection was not mentioned; one patient had "rheumatism" and several patients had nervous disturbances.

Of Becker's four cases, syphilis was definitely absent in three and its presence was very doubtful in one. The other patients had evidence of

1. Becker, S. W.: Generalized Telangiectasia, Arch. Dermat. & Syph. **14**:387 (Oct.) 1926.

focal infection, such as mastoiditis, tonsillitis, prostatitis and dental infection, and also showed toxic or degenerative changes which occasionally follow such infections, including nephritis, hypertension and diabetes.

No mention was made of treatment in any of the cases reviewed except Becker's case 2. The facies of this patient suggested congenital syphilis, although the blood and spinal fluid were normal. Under treatment with mercurial inunctions and potassium iodide, the telangiectasia improved a great deal. In case 1, the disease progressed; in case 3, the outcome was not stated, and in case 4, the patient died of an unknown cause.

In view of the obscure etiology and apparently unsatisfactory treatment for the condition considered in this article, it was felt that it might be worth while to report the following case in which a definite focus of infection was found, the successful treatment for which was followed by complete disappearance of the eruption.

## REPORT OF A CASE

*History.*—Sister E., aged 29, a nun who taught school, had a generalized eruption of one year's duration. She had had chronic sinus infection for four or five years, characterized by pain in the right antral region, postnasal mucous discharge and frequent colds. She had been under treatment for the sinuses for about a year. She complained that her head felt dull at times, although it had felt better recently. The tonsils had been removed ten years before. Roentgenograms of the teeth taken six months before were negative. She had had occasional attacks of gas in the stomach, especially after eating raw food. During the seven months before examination she had had three "spells," characterized by sudden swelling of the face, throat and hands, marked increase in the redness of the rash, and nausea and vomiting. The gastric symptoms usually lasted about two hours, the swelling about two days and the general flare-up of the skin about a week. The bowels usually moved daily without laxatives, although they tended to be loose during the aforementioned acute attacks. The appendix was removed four years before. She had never had jaundice. There was no abdominal pain, not even during the "attacks."

She was thought to have had tuberculosis about five years before, which was apparently arrested at the time of the examination. She had had an occasional pleural pain during the past four years, and had an occasional pain about the heart. About a month before this history was taken, she kept a temperature chart, making notations twice daily for a week; the highest temperature was 99 F.

There was no history of genito-urinary disorders; the menstrual periods were normal. There had been no recent urinalysis. She had had occasional soreness and stiffness of the wrists during the past four years. She had taken no drugs except occasionally milk of magnesia. The diet was not abnormal, except that she drank very little water and usually ate meat twice daily.

There was no mention of allergy in her family or in her own past history, with the exception of the angioneurotic edema-like swelling during the past seven months. About fifty food and bacterial allergens were tested, all of which were negative except Micrococcus catarrhalis, which gave a 2+ reaction.

The eruption ordinarily did not cause much discomfort, although at times it itched and produced a burning sensation.

*Examination.*—Examination of the skin revealed a generalized rash most pronounced on the upper part of the trunk and arms. The eruption was composed of capillary points and groups of points.

In some places these were scattered in a diffuse nondescript form; in other areas, groups of these capillary points were arranged in a vague reticular pattern with indistinct serpiginous or circular outlines about the size of a dime or smaller. There was no apparent involvement of the mucous membranes. A section of tissue was removed from the back for microscopic study. The following is a brief description of the histologic findings (Dr. Anderson):

The essential histologic changes were of a vascular nature, the epidermis and sebaceous glands being normal.

Under low power magnification, there was seen a rather marked perivascular cellular infiltration about all the blood vessels. This was more marked in the upper and middle cutis than in the deep cutis. There was also from a slight to moderate degree of interstitial edema in the subpapillary region.

Under high power magnification, the walls of the capillaries were definitely thickened, in some places the thickening being so marked as definitely to narrow the lumen. In others the thickened walls of the blood vessels tended to take on a homogeneous hyalinized appearance. In several instances in which the section had cut the vessels lengthwise, there was definite evidence of increased tortuosity. The perivascular cellular infiltrate was composed mainly of round cells and some endothelial cells.

The diagnostic impression was that the condition was an inflammatory capillaritis leading to telangiectasia and degenerative changes of the blood vessels.

Examination of the sinuses was made by Dr. Burrows.

No local treatment was given other than a bland shake lotion. Prior to the patient's coming under observation, two small openings had been made into the right antrum at different times, each operation being followed by temporary relief from the sinus symptoms. In August, 1930, an examination revealed some pus in the ethmoid region on both sides. The tonsils had been cleanly removed several years before. Roentgenograms of the teeth revealed them to be vital and in good condition. Roentgenograms of the sinuses showed the right antrum cloudy and the condition of the left frontal sinus questionable. The right antrum was hazy on transillumination, as were the ethmoids on both sides. The openings previously made into the antrum were closed.

The diagnosis was chronic infection of the right antrum and ethmoid sinuses bilaterally.

*Treatment.*—A moderate-sized opening was made into the right antrum. No pus was found. As before, relief lasted until the antrum closed, although the ethmoiditis responded rapidly to treatment with Dowling (solution of mild silver protein) packs. Later a stock-mixed, respiratory vaccine was used, which gave a little relief, but did not cure the patient after continued use.

In December, 1930, a large permanent window was made in the right antrum, which again gave the patient about the same relief that she had obtained before. The condition soon became stationary and remained so until April, 1931, when treatment was begun with autogenous vaccine. The vaccine, which contained Streptococcus viridans and Staphylococcus aureus, 10,000,000 of each per cubic centimeter, was given subcutaneously twice a week, beginning with 1 minim (0.06161 cc.) and increasing 1 minim each dose up to 20 minims (1.24 cc.), avoiding local and general reactions. Soon after the patient began the vaccine

therapy, the skin cleared up entirely. Gradually all other symptoms disappeared, except occasional mild headaches and some distress over the upper teeth on the right side, which seems to be improving satisfactorily.

## COMMENT

It is always unwise to argue *post hoc ergo propter hoc* on the findings in a single case, and yet the circumstantial evidence is certainly strong in this instance. A patient with a typical and extensive case of generalized telangiectasia suffered from a chronic sinus infection for at least five years. Seven months after the first dermatologic examination the patient reported again for observation. The improvement in the eruption was striking. During this time she had had local treatment for the infected sinuses, and a permanent window had been made in the right antrum. At this time washings from the right antrum were cultured on Löffler's medium. Streptococcus viridans and Staphylococcus aureus grew. Five hundredths of a cubic centimeter of heat-killed saline suspension of each of these organisms containing 500 bacteria per cubic centimeter was used as an antigen for an intradermal test, saline washings from sterile culture mediums being used as a control. Within twenty-four hours, a strongly positive reaction was observed at each test site, consisting of a red tender swelling about the size of a dollar. The control was negative. A vaccine was then prepared from the organisms and administered as has been described. Two and a half months later, the patient reported for observation again, and the eruption had entirely disappeared. The patient has remained well up to the time of writing or about two months. The disappearance of the rash coincident with the eradication of the chronic sinus infection does not prove a relationship between the two, but it seems sufficiently convincing to justify a thorough search for foci of infection in future cases of this disorder, and serious consideration should be given to the nasal sinuses as a possible source of trouble.

## CONCLUSIONS

A typical case of generalized telangiectasia is described in which complete disappearance of the eruption followed successful treatment for chronic sinusitis.

2007 Wilshire Boulevard

607 South Hill Street

# KERATOSIS FOLLICULARIS SINE DYSKERATOSIS

## A NEVOID ANOMALY OF DEVELOPMENT

### REPORT OF A CASE

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NEW YORK

Recently a patient was seen in consultation in the clinic with an eruption that appeared to fulfil clinically all the diagnostic criteria of keratosis follicularis (Darier). However, further study of the case, including microscopic examination of a biopsy specimen, proved my tentative diagnosis to be incorrect. Since I have not been able to find a description of a similar case in the literature and since this hitherto unknown dermatosis mimics not only Darier's disease but also other follicular disorders, I am tempted to report my case.

### REPORT OF CASE

*History.*—A. D., a white girl, a high school student, was born in New York eighteen years before examination. When she was 5 years of age, her mother noticed dirty brown areas on the patient's face, especially around the nose. No attention was paid to the eruption, for the mother was convinced that her daughter was suffering from a disorder of the skin that had afflicted not only the child's father but also her grandfather. Incidentally, an examination of the patient's father at a later date revealed the presence of Microsporon furfur in the pigmented patches on the trunk.

When 10 years old the patient sustained an attack of scarlet fever, with uneventful recovery. The following year menstruation set in. The menses had always been scanty and irregular. It had also been noted that the patient's features first became chubby about this time.

Since its onset the pigmentation had gradually enlarged, and had slowly extended downward to include the neck, shoulders, chest and back. Except for the progressive discoloration of the skin and the resulting cosmetic defect, there had been no discomfort or other subjective symptoms.

*Examination.*—The patient was well nourished and apparently obese. She was 56 inches (142.7 cm.) tall and weighed 169 pounds (76.6 Kg.). The skull was not deformed. There was no thinning of the hair. The eyes, ears and nose were essentially normal. The tonsils were hypertrophied. The lungs were clear. A systolic murmur was audible at the apex. The breasts were large and pendulous. The abdomen was protuberant and flabby. There was no tenderness or rigidity

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From the First Dermatological Division, Columbus Hospital.

of the abdominal muscles. The reflexes were not overactive. The pulse rate was 114; the blood pressure, 120 systolic and 64 diastolic. Consent for a pelvic examination was denied.

The skin presented a bizarre picture in that there were many linear, patchy, discrete or confluent, café-au-lait, dotted areas over the seborrheal regions of the body (on the scalp, face, neck and shoulders, over the sternum and along the spinal column) (fig. 1). The pigmented lesions were bandlike over the shoulders and streaky over the sternum and back. The eruption did not follow the lines of cleavage of the skin, nor did it display a definite pattern. It tended to be sym-

Fig. 1.—Note the distribution, arrangement and character of the eruption.

metrical and bilateral and involved, in addition to the seborrheal areas, also the extensor surfaces of both lower and upper extremities. Each streak, band or patch consisted of hyperpigmented skin, the follicles of which were hyperkeratotic, conical and deeply pigmented. The picture suggested that of Darier's disease. To the palpating finger the skin felt as though grains of sand had been sprinkled on its surface.

The follicles about the hair line, under the chin and on the back of the neck were larger and darker, and tended to coalesce; those in the remaining areas were smaller (the size of a pinhead) and light brown, and stood out as discrete conical elevations. Scattered here and there on the face, chest and back were a few acne papules.

Laboratory Examination: The urine showed a faint trace of albumin on repeated occasions, otherwise it was essentially normal. The Wassermann reaction of the blood was negative. Chemical examination of the blood yielded the following data; sugar, 128 mg.; nonprotein nitrogen, 35 mg.; urea nitrogen, 15 mg.; uric acid, 3.4 mg.; creatinine, 1.5 mg., and cholesterol, 185 mg. The basal metabolism was minus 18. Roentgen examination of the skull did not reveal any abnormality of the sella turcica.

Fig. 2.—Low power photomicrograph showing dilated mouth of follicle, lamellation of the corneous layer, prominent granular layer and mild congestion in the upper cutis.

Histologic Examination: A specimen was removed under local anesthesia from the back of the neck, near the hair line where the conical, brownish elevations were quite large. It was fixed, embedded and stained in the usual manner. Sections were studied with the assistance of D. L. Satenstein (figs. 2, 3, 4 and 5).

The epidermis was irregular throughout. The follicles were dilated and the follicular mouths were widened. The granular layer was well retained throughout the entire epidermis. The horny layer was laminated and slightly increased in the follicles.

The vessels were somewhat dilated. There was moderate edema of the subepidermic connective tissue. But few lymphocytes were noted in the perivascular lymphatic spaces. The infiltration was scattered. There was also a sparse cellular infiltration about the deeper portion of the follicular wall. The coil glands were markedly degenerated. There were no degenerations of the connective tissue and no elastic tissue changes. The pathologic picture suggested more an anomaly of development than a mild type of xerosis associated with follicular changes.

Fig. 3.—Section showing the irregular epidermis; the granular layer is well retained. A normal sebaceous gland and moderate edema of the subepidermic connective tissue are shown.

*Treatment.*—Owing to the fact that the pathologic changes as well as the clinical and metabolic investigations suggested an anomaly of development, associated with, if not directly caused by an endocrine dysfunction (thyroid?), as the etiologic basis of the patient's disorder, tablets containing all the various glands of internal secretion were prescribed. I felt that it would have been too tedious a process to try each gland preparation separately even though the thyroid apparently seemed at fault. In addition colloidal baths were suggested. After four months' treatment the basal metabolic rate became minus five, but there was no

apparent improvement in the appearance of the skin. Incidentally the patient did not lose any weight, nor was there an elevation in the pulse rate. She is still under treatment.

COMMENT

The differential diagnosis offered many difficulties. In the first place, the follicular character of the eruption, its distribution, its mode of

Fig. 4.—High power photomicrograph showing the well marked granular layer, lamellated horny layer and absence of corps ronds and grains.

onset and its chronic course pointed toward the diagnosis of keratosis follicularis (Darier [1]). However, the absence of palmar lesions, of the thick seborrheic-looking coating on the scalp, of fissuring, of irregular, papillomatous, confluent areas and of fatty central concretions weak-

1. Darier and Thibault: Thèse de Paris, 1889; Ann. de dermat. et syph. **10**:14 (July) 1889.

ened my initial impression as to the nature of the disorder. After the coup de grâce given by the pathologic examination, which did not reveal the presence of dyskeratosis, corps ronds and grains [2] which are distinctive changes of Darier's disease, the latter disorder could no longer be considered in the diagnosis.

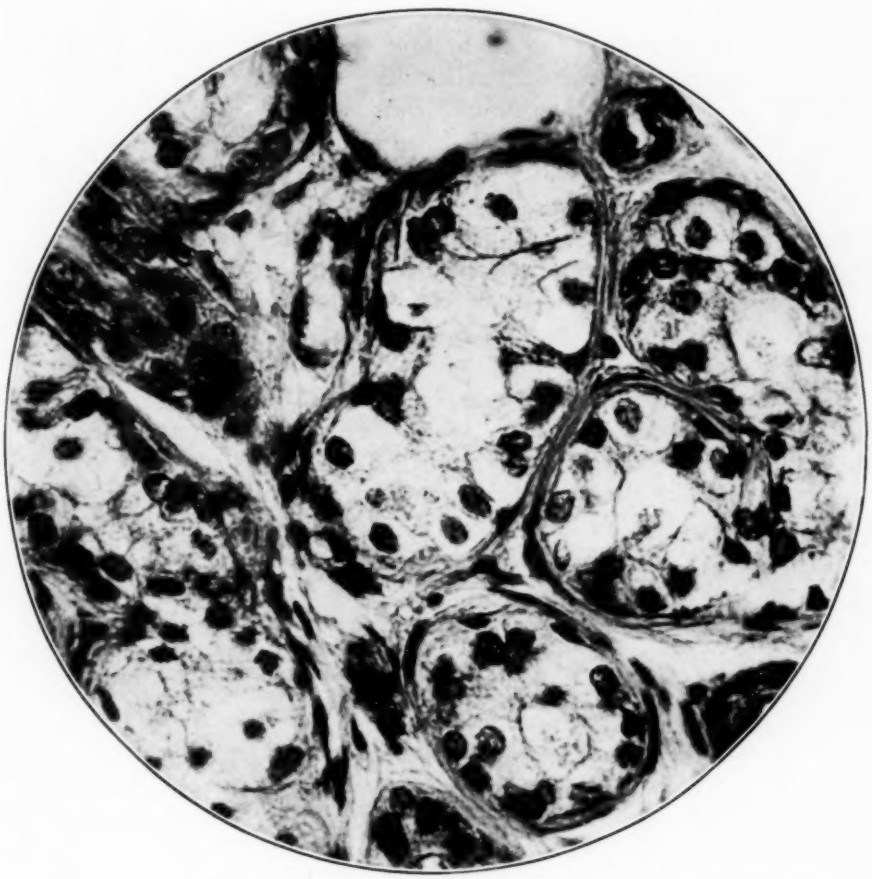

Fig. 5.—The epithelial lining of the coil glands is well broken up and disorganized.

Keratosis follicularis (lichen pilaris) was also untenable as a diagnosis, for this follicular disturbance is not only localized, as a rule, but is also characterized, among other changes, by retention cysts with the remains of poorly developed hairs.[3]

2. Ormerod and MacLeod: Brit. J. Dermat. **16**:32, 1904. MacCarthy, L.: Histopathology of Skin Diseases, St. Louis, C. V. Mosby Company, 1931, p. 102.

3. Morrow: Keratosis Follicularis, J. Cutan. Dis., 1886, vol. 4.

Kyrle's "keratosis in cutis penetrans" [4] with the characteristic horny plugs breaking through the epithelium at the base of the follicles and continuing to enlarge in the cutis could not be compared with the pathologic changes noted in this case. Moreover, in Kyrle's ichthyosis follicularis there are, in addition to the hyperkeratosis, funneling of the follicles, lamellation of the corneous layer and absence of the sebaceous glands. Figure 3 shows a well developed sebaceous gland.

In lichen spinulosus [5] there are three different areas of cornification: the follicle, sweat pore and interfollicular papules. Similar changes were not present in toto in the case under discussion.

The tuberculous structure of lichen scrofulosorum [6] alone would be sufficient to eliminate this toxic dermatosis in case of doubt.

Pityriasis rubra pilaris shows a progressive inflammatory process with marked perifollicular infiltration. Lichen ruber acuminatus shows, on the other hand, regressive inflammatory changes with a considerable polymorphous infiltration in the cutis.[7] Even without the aid of the clinical data, the experienced skin pathologist could readily differentiate these clinical entities from each other as well as from the present case.

In keratosis follicularis contagiosa (Brooke [8]) the inflammatory reaction is more marked than in the present case. Besides, if one disregards the pathologic criteria, the black points at the follicular outlets and the horny, spikelike elevations are seen only in Brooke's keratosis.

A widespread molluscum contagiosum should rarely confuse the novitiate.[9] However, the wide distribution, the lack of the soft central plug and the absence of the pearly-looking character of the so-called "molluscum bodies" should place the diagnostician on his guard. Likewise, the acuminate red papules of molluscum contagiosum miliare with tiny translucent centers "apparently at the sites of the pilosebaceous follicles" [10] should offer no difficulties.

Finally, the type of ichthyosis that has a preference for involvement of the follicle usually shows fine lanugo hairs coiled up in the mouth of the follicle. Additional features are: a peculiar type of cornification, atrophy of the papillae and atrophy of both coil and sebaceous glands.[11]

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4. Kyrle, J.: Vorlesungen über Histologie der menschlichen Haut und ihrer Erkrankungen, Berlin, Julius Springer, 1925, vol. 1; Hyperkeratose und Hyperpigmentation, Arch. f. Dermat. u. Syph. **104**:235, 1910.

5. MacCarthy (footnote 2, second reference, p. 114).

6. Satenstein, D. L.: Tuberculosis of the Skin, Arch. Dermat. & Syph. **23**: 309 (Feb.) 1931.

7. MacCarthy (footnote 2, second reference, pp. 217 and 219).

8. Brooke: International Atlas von seltener Hautkrankheiten, Hamburg, L. Voss, 1892.

9. Kingery, L. B.: Histogenesis of Molluscum Contagiosum, Arch. Dermat. & Syph. **2**:144 (Aug.) 1920.

10. Whitfield, A.: Brit. J. Dermat. **41**:10 (Jan.) 1929.

11. MacCarthy (footnote 2, second reference, p. 108).

SUMMARY

1. In a young white woman a bizarre eruption had developed on the face during childhood.

2. The lesions were conical, follicular, keratotic and pigmented. They were bilateral and symmetrical, and favored the seborrheal areas of the body.

3. An unusual pathologic feature was the absence of dyskeratosis, of corps ronds and of a marked inflammatory reaction.

4. The coil glands were broken down, a result of the process responsible for the pathologic changes.

5. The pathologic display suggested an anomaly of development, probably related to the endocrine disturbance noted clinically (thyroid?).

6. No improvement was noted with opotherapy during the short period of observation.

7. The title keratosis follicularis sine dyskeratosis—a nevoid anomaly of development—has been used in reporting my observations, as it suggests the change found.

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# LUPUS VULGARIS

## TREATMENT WITH PYROGALLOL ACCORDING TO THE METHOD OF VEIEL

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The favorable results that my father obtained in lupus vulgaris with the pyrogallol method induced me to continue along the same line of treatment, and as I have had the same success with my patients, I believe that my experience may be worthy of publication.

The treatment for lupus vulgaris with caustic substances, such as zinc chloride, potassium hydroxide, potassium permanganate, lactic acid, and many others, had long been known. Gradually the conviction gained ground that these caustics were for the most part not *elective;* they destroyed not only the lupus parts but also the healthy, unaffected surrounding tissue, and in this way there sometimes arose injuries that left ugly scars and keloids which appeared as a result of the caustic.

Apart from the fact that the therapeutic value of the medicaments was thereby greatly diminished, there was the disadvantage that despite the severe destructive action, the lupus did not entirely disappear and sooner or later recurred. The undestroyed remainder of the lupus, protected by keloid-like fibrous tissue, was then difficult to reach.

It was therefore meritorious of T. Veiel[1] to draw attention (in 1893) to the elective destructive action of pyrogallol in tuberculous diseases of the skin.

Pyrogallol, a trihydroxybenzene, is a colorless, strong reducing substance that withdraws oxygen from the skin and other organic tissues. This reducing action on the skin is accompanied by a violent dermatitis which appears all the more intense in less healthy skin; hence, tissue changed by lupus (especially in this instance) offers less resistance to caustic action and, as it were, melts away while the healthy tissue remains. The pathologically altered cells are destroyed, while the particles of tissue not yet affected become more prolific and, after the general expulsion, assume the task of closing the resulting wound.

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1. Veiel, T.: Zur Therapie des Lupus vulgaris, Berl. klin. Wchnschr. **30**:944, 1893.

In 1908, F. Veiel,[2] in a lengthy article, referred to the salutary action of pyrogallol. I apply the treatment almost entirely according to his method, which is as follows:

The cartilages of the ear and nose are covered with too thin a skin for one to apply pyrogallol ointment (pyrogallol 10, petrolatum album 90) with immunity for any length of time, so that if the lupus is localized there I sometimes rather advise treatment with Finsen light or radium. Yet case 18 is an example of the excellent result of treatment with pyrogallol ointment (10 per cent pyrogallol for more than a month at a time) in contrast with case 2 in which the process reached as far as the periosteum of the phalanx so that an underlying tendon was destroyed, resulting in a contraction of the flexor tendon. In case 2, treatment with x-rays or Finsen light would probably have been better.

As pyrogallol (especially in alkaline surroundings, e. g., serum) can easily be resorbed, it is advisable to guard against symptoms of poisoning, such as methemoglobinuria (green coloring of the urine), nephritis, etc. As salicylic acid promotes the resorption, I do not add it to the ointment, but use exclusively petrolatum album mixed with 10 per cent pyrogallol, with or without the addition of 1 or 2 per cent procaine hydrochloride. As already mentioned, the toxic action shows itself more in alkaline surroundings, for which reason Unna gave hydrochloric acid internally. Only in case 8 was hydrochloric acid given temporarily, as the surface suitable for resorption was extremely great. Yet in this patient who was treated in the outpatient service, like nearly all the other patients, no symptoms of poisoning appeared.

Before the treatment begins, the patient is first informed that his lesions, which look rather quiet and innocent, will become much larger and more painful during the treatment. It is certain that the Finsen method has an advantage over this treatment in that it causes the patient practically no pain, but, on the other hand, the radiation must be applied for a much longer period before success is obtained. This longer duration of treatment and the consequently higher cost are sometimes the reason that this method is not adopted, or if so, not fully. The cosmetic results of the Finsen method are not better than those of the pyrogallol method; moreover the number of recurrences that follow the latter is, in my opinion, no greater than that with the Finsen method.

With the pyrogallol method much depends on the patient's being informed in advance that he is going to begin a very unpleasant period of three or four months, which, however, will be well worth while. It is perfectly true that "it must first be worse before it can be better." So, after having pointed out to him the difficulties expected, I begin the

2. Veiel, Fritz: Zur Pyrogallol Behandlung des Lupus, Berl. klin. Wchnschr. **45**:313, 1908.

treatment with an ointment of 10 per cent pyrogallol in petrolatum album which, smeared on cotton bandages, is laid on the lupus spot once or, if possible, twice a day. In the first week the skin of the affected area swells exceedingly, becomes red and is sometimes covered with a grayish film. After from eight to twelve days there is an excessive serous discharge which, in the case of large areas, necessitates renewal of the bandage several times a day. One may expect a wound surface that appears twice as large as the original lupus area.

As the most striking example of an unexpected extension of destruction, I append some sketches of the upper part of the right arm of a

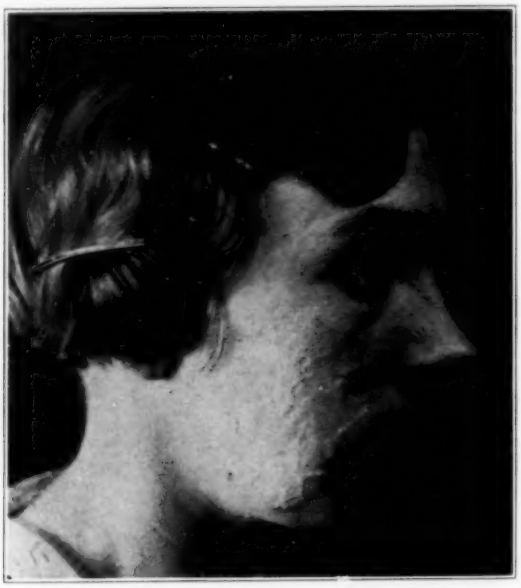

Fig. 1 (case 4).—Favorable cosmetic result seven years after treatment (Aug. 15, 1931).

woman (case 8) which show primarily three small lupus spots on the lower portion, whereas on the deltoid area a large lupus spot was situated (Jan. 1, 1924). After eighteen days' treatment with 10 per cent pyrogallol it appeared that the skin of the whole upper part of the arm was affected, the area measuring two palmbreadths (Feb. 9, 1924). Three weeks later the necrotic mass, 1 or 2 cm. in thickness, had already been expelled from the upper portion, but was still firmly attached to the lower portion. The aspect of the sore had been practically reversed: above, a comparatively quiet wound with small remainders of necrosis and numerous granulations; below, an enormously thick (from 2 to 3 cm.) necrotic mass of tissue firmly attached to the under layer and

discharging copiously. Six weeks later (April 16) the upper portion was practically healed, and the cavity in the lower part also showed granulations. Fourteen days later (April 29) general quick healing commenced with the application of 0.5 per cent pyrogallol ointment, and on June 1, one hundred and twenty-two days after the beginning of the treatment, the arm was healed.

Fig. 2 (case 8).—*A*, primary condition. *B*, appearance after eighteen days' treatment with 10 per cent pyrogallol. The whole lateral surface of the arm is inflamed. *C*, appearance after forty days' treatment with 10 per cent pyrogallol. In the upper part there are small necroses (black); in the lower part, a thick mass of necrosis. At this point, treatment with 2 per cent pyrogallol ointment began. *D*, appearance after six weeks' treatment with 2 per cent pyrogallol. The upper part shows small granulated patches (hatched areas) in the almost covered skin defect (dotted area); the lower part, a large granulated spot (hatched area). Treatment with 0.5 per cent pyrogallol was here begun. *E*, appearance after fourteen days' treatment with 0.5 per cent pyrogallol. Only a few granulations are visible.

This somewhat detailed description of a single case may serve to show that one cannot determine clinically in advance how far the lupus erup-

tion extends; case 8, as can be understood, caused much anxiety, but without hospitalization and without skin grafting the entire skin defect, which was almost two palmbreadths in size, closed completely. One would have thought that the greatest evil lay in the upper part of the arm, the obvious lupus patch, and that the three small spots were of

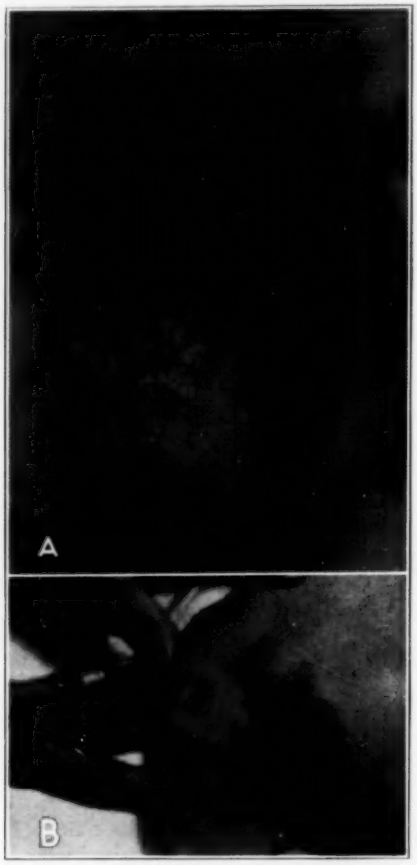


Fig. 3 (case 15).—*A*, primary condition of a lupus spot on the right buttock. *B*, ulcer after a month's treatment with 10 per cent pyrogallol.

secondary importance. The contrary turned out to be the case: The lower parts caused the greatest destruction and were longest in healing.

In my opinion, the advantage of the pyrogallol method over the Finsen and other radiation methods is obvious, because with the latter one would be inclined to give less attention and time to the smaller spots than to the larger ones, whereas the biologic reaction to the pyrogallol showed the contrary to be necessary. With the pyrogallol destruction

Fig. 4 (case 21).—*A*, primary condition (April 20, 1931). *B*, appearance after fourteen days' treatment with 10 per cent pyrogallol (May 5). A border of zinc paste has been placed around the wound. *C*, appearance at the end of the treatment with 10 per cent pyrogallol and at the commencement of treatment with 2 per cent pyrogallol ointment (May 23). *D*, quick healing and expulsion of the necrosis after seventeen days' treatment with 2 per cent pyrogallol (June 9). *E*, appearance of totally healed area (August 20).

one also reaches the latent lupus spots, which are not yet clinically recognizable. The pyrogallol itself seeks all the diseased tissue, as it were, and destroys that in a far better way than the dermatologist himself could.

As exposure of the wound, covered with pyrogallol ointment, to the air is sometimes very painful, the renewal of the ointment must be done not only quickly but also with the necessary ointment bandages prepared in advance, so that after the cleansing of the serous wound surface, they can be applied immediately. Should the healthy area surrounding the sore, which begins to define itself after a few days, unexpectedly show symptoms of dermatitis, a simple layer of resorcinol paste around the wound is sufficient to put a stop to them. A layer of ointment the thickness of a knife must be smeared on the bandages with a spatula of glass or wood, as with a metal spatula chemical compounds arise that

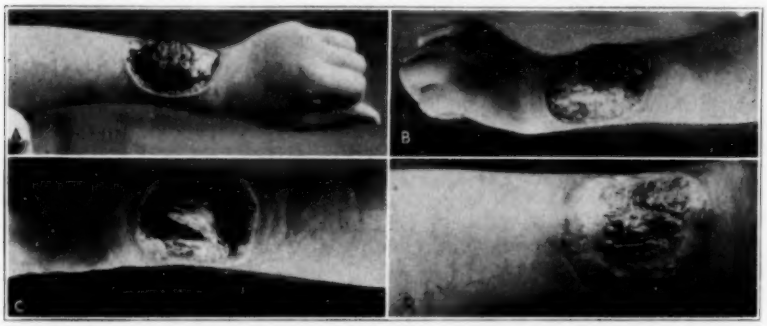

Fig. 5 (case 22).—*A*, necrosis on Jan. 10, 1932, after the application of boric acid ointment for six days. Previously 10 per cent pyrogallol ointment (including 2 per cent procaine hydrochloride) had been used for six weeks, followed by 2 per cent pyrogallol ointment. *B*, exposed tendon of the extensor carpi ulnaris (January 10). *C*, necrotic tendon of the extensor carpi ulnaris (January 24). Boric acid ointment was being used. *D*, the wound has nearly closed (February 24) under treatment with boric acid ointment.

diminish the action of the pyrogallol. Occasionally it is necessary to add procaine hydrochloride, from 1 to 2 per cent, to the ointment, as daily contact with the patient and some persuasion are usually sufficient to convince him that the rigorous action of the ointment is necessary to burn out the deeply situated tuberculous process entirely. The application of the 10 per cent pyrogallol for one month is sufficient for the distinct demarcation of the tissue to be eradicated. The original small lupus spot is seen as a black, ugly (and if it is large, as a malodorous) tumor, from two to two and a half times larger, discharging serous and purulent matter. It is practical sometimes to cut off superficially larger, necrotic pieces of tissue, which, saturated with pyrogallol, are of a

grayish color; the healing of the wound will be somewhat accelerated. This does not hurt, nor is there any bleeding, as the tissue is a stiff collagen mass. The 2 per cent pyrogallol ointment is used the second month, and the painfulness becomes much less by the end of this period; moreover, the patient himself notices that the necrotic tissue, cleanly defined, is rising out of the wound, which again encourages him to continue the treatment. The third month the wound closes under treatment with 0.5 per cent pyrogallol ointment and the painfulness disappears altogether.

This is the pyrogallol treatment, shown somewhat schematically; the various periods may be longer or shorter, although a shorter period than thirty days for the application of 10 per cent pyrogallol is never

*Data on Patients Treated for Lupus Vulgaris by Pyrogallol Method*

| Case | Patient | Sex | Age | Duration of Disease | Site of Lupus | Duration of Treatment, Days | Lapse of Time Since Cure Was Established, Years |
|---|---|---|---|---|---|---|---|
| 1 | B. | M | 47 | 13 yr. | Whole face | 112 | 25 |
| 2 | H. | F | 34 | 3 mo. | Middle finger of right hand | 210 | 8 |
| 3 | R. | F | 29 | 10 yr. | Left cheek, left knee | 52 | 7 |
| 4 | R. | F | 21 | 5 yr. | Right cheek | 56 | 7 |
| 5 | G. | F | 17 | 4 yr. | Nose and upper lip | 83 | 7 |
| 6 | S. | F | 27 | 2 yr. | Left cheek | 104 | 4½ |
| 7 | B. | M | 19 | 5 yr. | Right side of neck | 110 | 4½ |
| 8 | J. | F | 40 | 30 yr. | Right upper arm | 122 | 4 |
| 9 | S. | F | 40 | 28 yr. | Right cheek; under lip | 105 | 4 |
| 10 | T. | F | 44 | 22 yr. | Left upper arm | 200 | 4 |
| 11 | V. | F | 25 | 1 yr. | Face (right side of jaw) | 120 | 3 |
| 12 | W. | F | 20 | 9 yr. | Right side of neck and chin | 98 | 3 |
| 13 | B. | M | 3 | 2 mo. | Glands of left side of neck | 108 | 2 |
| 14 | B. | F | 46 | 10 yr. | Right cheek | 126 | 2 |
| 15 | K. | M | 4½ | 2 yr. | Right buttock; right thigh; left forearm | 120 | 2 |
| 16 | v. D. | M | 18 | 2 yr. | Left cheek | 115 | 1½ |
| 17 | V. | M | 12 | 10 yr. | Right cheek | 142 | 1½ |
| 18 | L. | M | 16 | 10 yr. | Nose, upper lip, right cheek | 113 | 1 |
| 19 | v. a. K. | F | 21 | 8 yr. | Right cheek | 67, 75, 240 | 1 |
| 20 | M. | F | 55 | 4 mo. | Right cheek | 77 | ½ |
| 21 | d. J. | M | 28 | 22 yr. | Left cheek | 70 | ½ |

advisable. The most difficult part of the whole treatment is for the patient to have an originally rather mild lupus spot, which causes him practically no trouble, turned into a large painful wound with a great bandage and all the bother connected with it. Yet there is something encouraging in the pyrogallol treatment. After some time the patient himself sees the progress made; during the last weeks, especially, the healing is quickly progressive, the bandage becomes smaller and smaller and the pain disappears, all of which encourages him to persevere.

My opinion is that a gradual closing of the wound gives more likelihood of a soft supple scar than a too rapid epithelization, for which reason I sometimes prolong the period of application of the 2 per cent pyrogallol ointment a little more than a month.

As after-treatment I always prescribe the use of cod liver oil and, as a general strengthening therapy, sun baths if the patients are in the

position to take them. Periodic examination of the scars for some considerable time is always to be recommended; should any suspicious spots appear in the scar (diascopy), radium is used. It is hoped that the reading of this article will engender the desire among some dermatologists to employ this old, well tried method. In my opinion it deserves every recommendation and is as good as any other method, although, of course, others may be useful in certain cases.

### OBSERVATIONS

The accompanying table comprises some of the cases in which treatment has been given, arranged according to the lapse of time since the cure was established.

Case 1.—This patient was treated once or twice with radium and X-rays for slight recurrences. On the whole, the success of his first treatment, resulting in a practically complete cure, has been maintained.

Case 2.—The condition healed with destruction of the extensor tendon of the second phalanx of the middle finger of the right hand, whereby an antagonist action of the flexor tendon took place so that the finger, although free from lupus, assumed a vicious position of contraction, an evil that could have been corrected by surgical means; this, however, was not desired by the patient. The contraction did not affect the patient's ability to carry on her occupation as telephone operator.

Case 4.—Figure 1 shows good final results.

Cases 8, 10 and 11.—After a lapse of four, four and three years, respectively, these cases showed a slight recurrence, which was completely cured with radium.

Case 13.—This was not typical lupus but a large scrofuloderm proceeding from the neck glands, which, after having expelled an enormous piece of necrotic tissue, healed completely. In the beginning, thrombus of the large blood vessels of the neck or a pinching of the nerves was feared, but following excellent nursing in the Juliana Child Hospital, the child was cured.

Case 15.—Figure 3 shows the primary condition and the appearance after a month's treatment with 10 per cent pyrogallol ointment. One can see the pinched-out appearance of the ulcer after the expulsion of the necrotic tissue.

Case 18.—In this case of lupus papillomatosus the nose was covered with a layer of lupus tissue of the thickness of orange-skin. After the treatment the patient had a normal, though a red nose.

Case 19.—This patient has been under treatment for four years. She is a girl aged 20 years who gives the impression of a child of 14. Although the pyrogallol works well, there are continual recurrences, probably due to the poorly nourished condition of the patient.

Case 21.—Figure 4 shows the results of treatment in this case of lupus exfoliativus.

The following case (fig. 5) may serve as a warning that there should be the utmost precaution and careful control in the application of pyrogallol ointment in the vicinity of joints or tendons, generally speaking, on spots where there is but little underlying tissue.

CASE 22.—In a postman, 36 years old, treatment with a 10 per cent pyrogallol ointment containing 2 per cent procaine hydrochloride was begun on Nov. 17, 1931, for a large lupus spot on the left forearm. A regular four-day control period effected the desired necrosis, and on December 24, 2 per cent pyrogallol ointment was given. The patient then insisted on working, and remained away until Jan. 4, 1932. If the wound had become more painful during this time, the patient would have returned sooner and the destruction would not have been so severe. On his return I was alarmed to notice that the tendon of the extensor carpi ulnaris was completely exposed in the wound, with the result that the tendon necrosed. Luckily, no further disadvantages resulted from this treatment except a tender scar, which was strengthened by Braun's implantation of very small pieces of epithelium; this procedure will probably enable the patient to continue working without being troubled by the scar.

The patient's staying away from control observation for ten days and the adding of 2 per cent procaine hydrochloride to the 10 per cent pyrogallol ointment were the cause of this undesired course. I must therefore advise against the addition of procaine hydrochloride to the ointment for use on parts where there is little subcutaneous tissue, such as over joints or superficial tendons. In any case the patient must be examined every other day.

## SUMMARY

The old-fashioned Veiel treatment for lupus vulgaris with pyrogallol is to be recommended because it is economical and easily carried out. Its special advantages are the favorable cosmetic results, the comparatively short period of treatment and the few recurrences.

# ERYTHEMA NODOSUM

## CHARACTER AND ETIOLOGY

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AND
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### ETIOLOGY

The exact character and the cause of erythema nodosum have not been finally established. Opinion is divided between three suppositions; namely, that erythema nodosum is a manifestation of rheumatic fever; that it is a tuberculous manifestation or that it is an independent and separate disease probably of an acute infectious character.

The opinion that erythema nodosum is related to rheumatic fever has few supporters. Acknowledged differences in the manifestations of these diseases make it improbable that they are closely related. Koch [1] noted that 76 per cent of his cases occurred during the first six months and 24 per cent during the last six months of the year. In contrast to this, 52 per cent and 48 per cent of cases of rheumatic fever occurred in the corresponding periods. Thus erythema nodosum has a definite seasonal occurrence, which is not a feature of rheumatic fever. In none of Koch's forty-eight cases of erythema nodosum was there articular involvement. He noted the entire absence of chorea in erythema nodosum, and concluded there is complete lack of evidence of any relationship between it and rheumatic fever. Symes [2] noted that recurrences are rare in erythema nodosum; this disease usually leaves a permanent immunity. In contrast, recurrences of rheumatic fever are usual. He noted that endocarditis rarely occurs in erythema nodosum, but that it is a characteristic feature in rheumatic fever. Symes found no basis for the belief that erythema nodosum is related to rheumatic fever.

It is the opinion of many that erythema nodosum is related to tuberculosis, but there is no agreement on the nature of the relationship. Hamburger [3] believes erythema nodosum to be an especial form of tuberculid.

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From the Departments of Pathology and of Dermatology, Jefferson Medical College.

This work was made possible by funds from the Martin Research Foundation.

1. Koch: Ztschr. f. Kinderh. **40**:584, 1925.

2. Symes, J. O.: Brit. M. J. **2**:741, 1921; Lancet **2**:1033, 1929.

3. Hamburger: Handbuch der Kinderheilkunde, ed. 3, Leipzig, Pfaundler & Schlossman, 1923, vol. 2, p. 481.

Ernberg [4] interprets it as an anaphylactic manifestation produced by tuberculous protein set free in the patient's system—"an autogenous tuberculin reaction." Liebermeister [5] considers that erythema nodosum is a characteristic exanthematous eruption of secondary tuberculosis. Some believe that erythema nodosum occurs exclusively in susceptible persons freshly infected with a massive tuberculous inoculation. Wallgren [6] believes that erythema nodosum is an allergic reaction in such cases. Kundratitz [7] believes it to be a manifestation of tuberculosis "esophylactic in nature" in such cases. Feer [8] believes that erythema nodosum is itself an independent disease, but that tuberculosis constitutes an almost indispensible predisposing cause for its development. Others interpret erythema nodosum as a tuberculotoxic manifestation, and still others hold that it is a manifestation of tubercle bacillemia.

In reviewing these articles, one is struck by the theoretical character of the discussion, by the lack of experimental evidence and by the lack of essential objectivity. When systematic investigations have been made, evidences of active tuberculous disease have been found in only a small number of cases of erythema nodosum. Uffelmann [9] found evidences of active tuberculosis in 3 of 17 cases of erythema nodosum; Mackenzie [10] in 2 of 115 cases; Pollak [11] in 3 of 45 cases; Koch [1] in 5 of 48 cases; Hegler [12] in 3 of 45 cases; Bucher [13] in 1 of 44 cases; Gueissaz [14] in 14 of 300 cases; Vetleson [15] in 6 of 45 cases; Comby [16] in 14 of 170 cases; Lendon [17] in 2 of 124 cases, and Schapiro [18] in none of his 93 cases.

Reports from tuberculosis sanatoriums do not indicate that erythema nodosum is of frequent occurrence among tuberculous patients. Hegler found 1 case of erythema nodosum in 1,000 patients with tuberculosis;

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4. Ernberg: Jahrb. f. Kinderh. **45**:1, 1921.

5. Liebermeister, G.: Tuberkulose, Berlin, Julius Springer, 1921.

6. Wallgren: Beitr. z. Klin. d. Tuberk. **54**:143, 1922; Acta paediat. **5**:225, 1926; Jahrb. f. Kinderh. **117**:257, 1927.

7. Kundratitz: Jahrb. f. Kinderh. **63**:155, 1926.

8. Feer: Schweiz. med. Wchnschr. **56**:682, 1926.

9. Uffelmann, quoted by Tachau, in Jadassohn: Handbuch der Haut- und Geschlechtskrankheiten, Berlin, Julius Springer, 1928, vol. 6, p. 634.

10. Mackenzie, quoted by Tachau (footnote 9).

11. Pollak: Wien. klin. Wchnschr. **25**:1223, 1912.

12. Hegler: Ergebn. d. inn. Med. u. Kinderh. **12**:620, 1913.

13. Bucher: Inaug. Dis., Zurich, 1909.

14. Gueissaz: Rev. méd. de la Suisse Rom. **42**:706, 1922.

15. Vetleson: Tubercle **3**:433, 1921.

16. Comby: Progrès méd. **35**:633, 1922.

17. Lendon: Brit. M. J. **1**:165 and 651, 1925; Nodal Fever, London, Ballière, Tindall & Cox, 1905.

18. Schapiro: Beziehung zwischen Erythema Nodosum und Tuberculose, Breslau, Bres. Genossensch. Buckdr., 1920.

Schumacher [19] found 1 in 1,500 tuberculous patients; Gueissaz found none in 500, and Vetleson found 12 in 1,317 cases.

Feer,[8] Perel,[20] Pollak,[11] Troisier,[21] Vetleson and others inoculated animals with material taken from the nodules of erythema nodosum. In none of the animals did tuberculous lesions develop. We have found no record of positive results following such inoculation.

The most important evidence of a relationship between these diseases is that in a high percentage of cases of erythema nodosum, a positive reaction to the tuberculin test of the skin is obtained. Evidences of active tuberculosis are found as frequently among syphilitic persons as they are in those with erythema nodosum. A high percentage of syphilitic patients respond positively to the tuberculin test of the skin. Sometimes the cutaneous lesions of tuberculosis and syphilis are similar. Should one conclude from this evidence that syphilis is a manifestation of tuberculosis? This reference to syphilis is made merely to emphasize the necessity for controlled observations and for objectivity of attitude.

Tachau [22] has summarized the voluminous literature on erythema nodosum in a forty-six-page review of the subject. He devoted twelve pages to the evidence on the relationship of erythema nodosum to tuberculosis. He found himself in agreement with Bucher, Comby, Crosse, Demieville, Faerber and Boddin, Feer, Hegler, Hutinel, Jadassohn, Kleinschmidt, Mallein, Moro, Ochsenius, Paulouch, Rousseau, Schapiro, Schumacher, Volk and others in concluding that a foundation of evidence for the tuberculous nature of erythema nodosum had not been presented, and agreed with them in rejecting the view that erythema nodosum may be a tuberculous condition.

The opinion that erythema nodosum is an independent disease having the characteristics of an acute infectious fever rests almost entirely on the clinical manifestations of the disease. J. O. Symes has supported this opinion in several articles. He reported epidemic outbreaks, and expressed the belief that erythema nodosum is a specific infectious fever because of the evidence of its communicability, the occasional occurrence of epidemic outbreaks, the seasonal and age incidence and the order of events during the illness. This includes the incubation period, the prodromal period, the febrile reaction with leukocytosis, low blood pressure and cutaneous manifestations, the convalescence, the occasional relapses and, finally, the lasting immunity. These features are those seen in infections. In cases following known contact he found an incubation period of from nine to fifteen days before the onset of symptoms. The cutaneous nodes usually made their appearance from

19. Schumacher: Ztschr. f. Tuberk. **21**:468, 1914.
20. Perel: Monatschr. f. prakt. Dermat. **53**:463, 1911.
21. Troisier: J. de méd. et chir. prat. **93**:784, 1922.
22. Tachau (footnote 9).

three to five days after the onset. He expressed the belief that the absence of sunlight during winter months lowers the resistance and causes the increased incidence in the early months of the year. He believed that the tonsils and throat were the avenue of entrance of the infection. Lendon [17] reached the same conclusion as Symes. His recent study of ninety-six cases brought forth no evidence of a relationship to tuberculosis, and he regarded erythema nodosum as a specific infectious disease. Mitman [23] reported five cases occurring almost simultaneously in a small district, 2 of them following direct contact with other cases. Acute inflammation of the throat caused the diagnosis in four of the five cases to be tonsillitis prior to the development of the cutaneous lesions. Wallgren reported eighteen cases occurring in an epidemic among children in a school class of thirty-two. Kessinger [24] reported the epidemic occurrence of 9 cases among 51 inmates of a children's home. Tachau's review of erythema nodosum refers to thirty-five similar reports on epidemics of this disease.

With a few exceptions, bacteriologic studies of erythema nodosum have given negative results. Rosenow [25] reported the cultivation of organisms in seven cases. Cultures were made from excised portions of cutaneous lesions and, in some cases, from adjacent lymph nodes, the blood, the tonsils and diseased teeth. He reported the cultivation of the same type of bacteria in each case. In some cases streptococci were also cultivated. The organisms were pleomorphic bacilli showing clubbed and granular forms and forms indistinguishable from cocci. They occurred in irregular clumps and masses. They stained by Gram's method and were not acid-fast. They grew readily under aerobic conditions. When injected intravenously into animals, lesions having the characteristics and location of those of erythema nodosum resulted. He demonstrated the presence of these organisms in sections of lesions both from human beings and from animals. He believed those organisms to be the cause of erythema nodosum, and that diseased teeth and tonsils serve as portals of entry for the infection. These results have not been reproduced by others, and we have failed to find any record of investigations of this disease made by a similar technic.

## REPORT OF CASES

An opportunity for bacteriologic and histologic studies was presented in three cases of erythema nodosum.

CASE 1.—In R. B., a white woman, aged 19, a nurse, prodromal symptoms consisting of general malaise and pain about the knees were present for three days. The temperature was irregular, with a maximum elevation of 3 degrees. Approxi-

23. Mitman: Lancet **2**:751, 1927.
24. Kessinger: München. med. Wchnschr. **75**:1365, 1928.
25. Rosenow: J. Infect. Dis. **16**:367, 1915.

mately ten nodes developed simultaneously in the skin of the anterior tibial surfaces. These nodes had the typical characteristics of erythema nodosum, and the condition followed the usual course, disappearing entirely within ten days. Roentgen examination of the teeth showed rarefaction involving the apex of the second right molar, which was extracted. Cultures taken from the inflamed periapical tissue gave the same organism that was found in cultures of sections from the cutaneous lesion. The case presented no other features of interest.

A piece of skin and subcutaneous tissue, approximately 1.2 by 0.4 cm. and 0.5 cm. deep, was excised from the center of a cutaneous node, under strict surgical asepsis. Material for inoculations was obtained by scraping the subcutaneous tissue and deeper portion of the dermis with a sterile knife. Neither the epidermis nor the dermis immediately adjacent to it was planted in the cultures. Cultures were made in hormone broth, a semisolid medium and brain broth, and shake cultures were grown in deep tubes of melted hormone agar to which ascites fluid had been added. Also blood agar plates were streaked. All culture mediums had been adjusted to $p_H$ 7.6. Twenty-four hours later, there was a moderate amount of

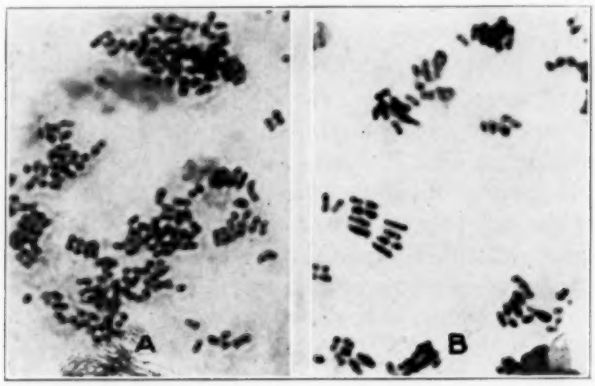


Fig. 1 (case 3).—A pure culture of the organism cultivated. *A*, a broth culture showing coccoid and bacillary forms. Capsules were demonstrable in recently isolated strains growing in broth. A transfer of this culture to a solid medium gave the forms shown in *B*. Both *A* and *B* were from cultures twenty-four hours old; methylene blue stain; × 1,800.

flocculent growth in the broth and in the semisolid medium. This consisted of organisms, varying greatly in morphology and adhering in small compact clumps (fig. 1). There were round forms indistinguishable from cocci, short plump, densely-staining rods and longer rods containing densely-staining granules. There were also irregular wedge-shaped forms. Capsules were demonstrated in fluid mediums but not in growth on solid mediums. These organisms stained by Gram's method and were not acid-fast. A less abundant growth of the same organism was present on the blood agar plates. The colonies produced no hemolysis, but had a distinct greenish cast in transmitted light. Colonies developed in the superficial portion of the deep agar tubes, but not in the deeper portions. No other organism occurred in any of the cultures.

The organisms were nonmotile. They produced no pigment and did not liquefy gelatin or acidify milk. No change was produced on mannite, dextrose, levulose, lactose, saccharose, maltose or galactose.

This organism does not conform exactly to the characteristics of any species described in Bergey's "Manual of Determinative Bacteriology." [26] A culture sent to Dr. Bergey for study [27] was reported to conform most to the characteristics of Corynebacterium lymphophilum. However, that species is nonpathogenic to laboratory animals; it is anaerobic and ferments dextrose. The organism from erythema nodosum produced lesions in animals, as will be shown. It is aerobic and does not ferment dextrose. These differences appear sufficient to distinguish this organism from Corynebacterium lymphophilum.

Case 2.—In R. W., a white woman, aged 21, the condition was of unusual severity and eventually ended fatally. The onset occurred with chills and fever, which persisted for two weeks prior to admission to the hospital. On admission the complaints were headache, pains in the limbs, a slight cough and marked weakness and malaise. The temperature ranged from 102 to 104.6 F. Examination of the blood on admission showed: hemoglobin, 85 per cent; red cells, 4,870,000; white cells, 4,000, of which 65 per cent were polymorphonuclears and 32 per cent

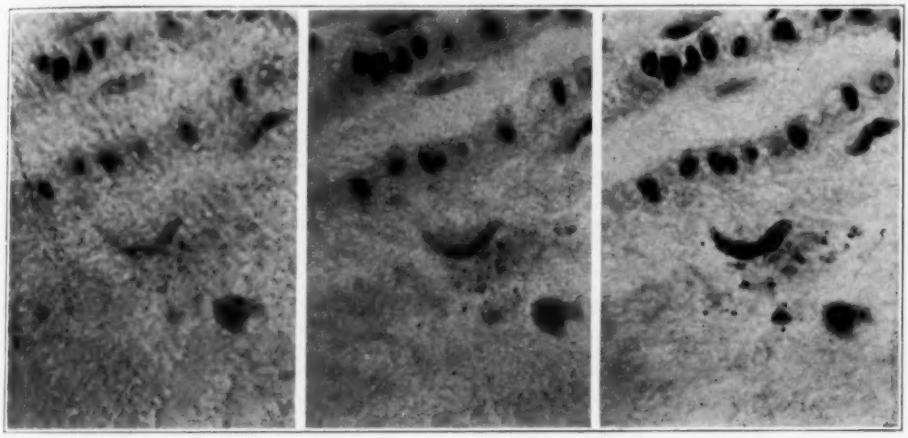

Fig. 2 (case 2).—Area of infiltration adjacent to an arteriole in the subcutaneous tissue. Numerous coccoid and a few bacillary forms were seen in this tissue. This figure shows three photomicrographs of the same field taken at different focal levels. Biopsy specimen, Zenker fixation, paraffin section; Gram stain; × 1,000.

lymphocytes. There was a gradual decrease in these elements. Two months later, examination showed 58 per cent hemoglobin, 2,820,000 red cells and 2,300 white cells. There appeared multiple erythematous areas from 1.5 cm. to 4 cm. in diameter, over the legs and arms. With their appearance there was an exacerbation of general symptoms. As these areas became nodular, fresh areas of a purpuric character developed on the limbs and trunk. Such areas appeared also on the neck and face. No portion of the body was free. The number of nodules present at one time was estimated above 200. The urine contained albumin, red cells and

26. Bergey: Manual of Determinative Bacteriology, ed. 3, Baltimore, Williams & Wilkins, 1930, p. 510.

27. Bergey: Personal communication.

mately ten nodes developed simultaneously in the skin of the anterior tibial surfaces. These nodes had the typical characteristics of erythema nodosum, and the condition followed the usual course, disappearing entirely within ten days. Roentgen examination of the teeth showed rarefaction involving the apex of the second right molar, which was extracted. Cultures taken from the inflamed periapical tissue gave the same organism that was found in cultures of sections from the cutaneous lesion. The case presented no other features of interest.

A piece of skin and subcutaneous tissue, approximately 1.2 by 0.4 cm. and 0.5 cm. deep, was excised from the center of a cutaneous node, under strict surgical asepsis. Material for inoculations was obtained by scraping the subcutaneous tissue and deeper portion of the dermis with a sterile knife. Neither the epidermis nor the dermis immediately adjacent to it was planted in the cultures. Cultures were made in hormone broth, a semisolid medium and brain broth, and shake cultures were grown in deep tubes of melted hormone agar to which ascites fluid had been added. Also blood agar plates were streaked. All culture mediums had been adjusted to $p_H$ 7.6. Twenty-four hours later, there was a moderate amount of

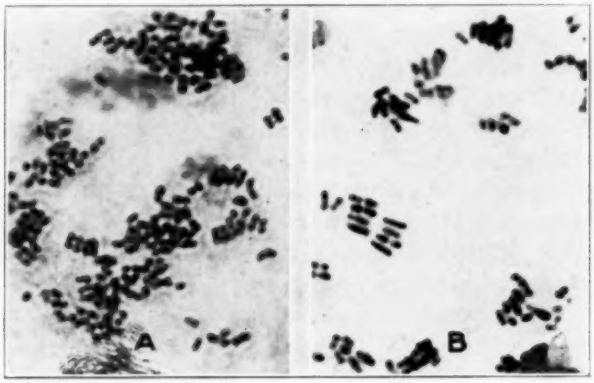


Fig. 1 (case 3).—A pure culture of the organism cultivated. *A*, a broth culture showing coccoid and bacillary forms. Capsules were demonstrable in recently isolated strains growing in broth. A transfer of this culture to a solid medium gave the forms shown in *B*. Both *A* and *B* were from cultures twenty-four hours old; methylene blue stain; × 1,800.

flocculent growth in the broth and in the semisolid medium. This consisted of organisms, varying greatly in morphology and adhering in small compact clumps (fig. 1). There were round forms indistinguishable from cocci, short plump, densely-staining rods and longer rods containing densely-staining granules. There were also irregular wedge-shaped forms. Capsules were demonstrated in fluid mediums but not in growth on solid mediums. These organisms stained by Gram's method and were not acid-fast. A less abundant growth of the same organism was present on the blood agar plates. The colonies produced no hemolysis, but had a distinct greenish cast in transmitted light. Colonies developed in the superficial portion of the deep agar tubes, but not in the deeper portions. No other organism occurred in any of the cultures.

The organisms were nonmotile. They produced no pigment and did not liquefy gelatin or acidify milk. No change was produced on mannite, dextrose, levulose, lactose, saccharose, maltose or galactose.

This organism does not conform exactly to the characteristics of any species described in Bergey's "Manual of Determinative Bacteriology." [26] A culture sent to Dr. Bergey for study [27] was reported to conform most to the characteristics of Corynebacterium lymphophilum. However, that species is nonpathogenic to laboratory animals; it is anaerobic and ferments dextrose. The organism from erythema nodosum produced lesions in animals, as will be shown. It is aerobic and does not ferment dextrose. These differences appear sufficient to distinguish this organism from Corynebacterium lymphophilum.

CASE 2.—In R. W., a white woman, aged 21, the condition was of unusual severity and eventually ended fatally. The onset occurred with chills and fever, which persisted for two weeks prior to admission to the hospital. On admission the complaints were headache, pains in the limbs, a slight cough and marked weakness and malaise. The temperature ranged from 102 to 104.6 F. Examination of the blood on admission showed: hemoglobin, 85 per cent; red cells, 4,870,000; white cells, 4,000, of which 65 per cent were polymorphonuclears and 32 per cent

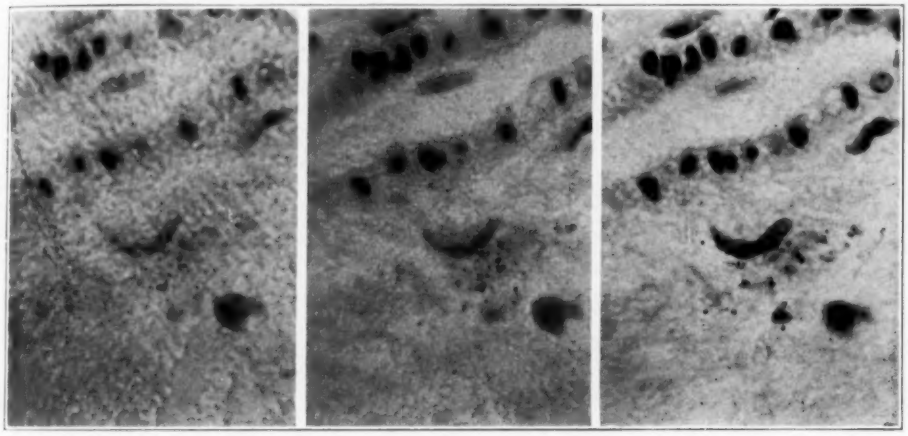

Fig. 2 (case 2).—Area of infiltration adjacent to an arteriole in the subcutaneous tissue. Numerous coccoid and a few bacillary forms were seen in this tissue. This figure shows three photomicrographs of the same field taken at different focal levels. Biopsy specimen, Zenker fixation, paraffin section; Gram stain; × 1,000.

lymphocytes. There was a gradual decrease in these elements. Two months later, examination showed 58 per cent hemoglobin, 2,820,000 red cells and 2,300 white cells. There appeared multiple erythematous areas from 1.5 cm. to 4 cm. in diameter, over the legs and arms. With their appearance there was an exacerbation of general symptoms. As these areas became nodular, fresh areas of a purpuric character developed on the limbs and trunk. Such areas appeared also on the neck and face. No portion of the body was free. The number of nodules present at one time was estimated above 200. The urine contained albumin, red cells and

26. Bergey: Manual of Determinative Bacteriology, ed. 3, Baltimore, Williams & Wilkins, 1930, p. 510.

27. Bergey: Personal communication.

débris. The curve for temperature became septic, and marked icterus developed. The nodules did not spread or develop into suppurative lesions, but their involution was slow, and fresh crops of nodules appeared from time to time. The patient gradually lost ground, and died nine weeks after admission. Permission for post-mortem examination was denied. This case was an instance of the fulminating or ominous type of erythema nodosum of which there are occasional accounts.

Under aseptic conditions about 10 cc. of blood from a vein of the arm was drawn into a sterile solution of sodium citrate. This was then planted in flasks of hormone broth and deep tubes of melted agar. About 1 cc. of blood was mixed with melted agar and poured into plates. After eighteen hours of incubation, organisms conforming in all particulars to the characteristics of the organisms

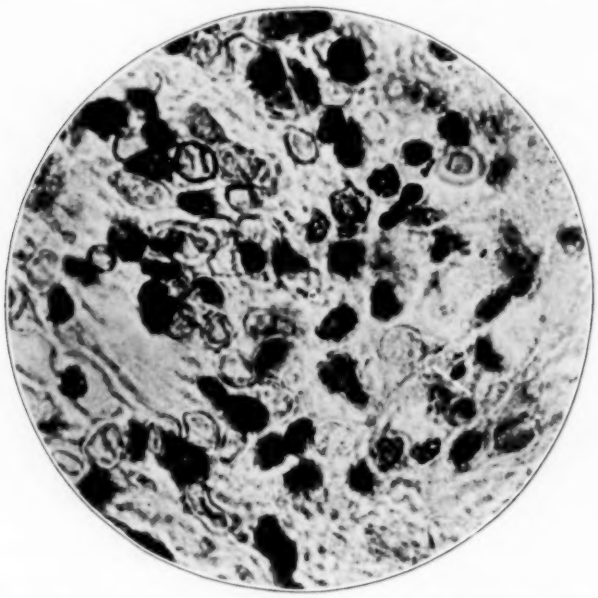

Fig. 3 (case 3).—Subcutaneous area of infiltration in a recently developed node. Coccoid and bacillary forms are seen in this tissue but are not so numerous as in case 2. Biopsy specimen, Zenker fixation, paraffin section; Gram stain; × 1,000.

cultivated in case 1 were found in the broth. Later they were found also in the aerobic portion of the deep agar tubes and in the blood agar plates.

Eleven days later a portion of a cutaneous node was excised and cultured as described in the report of case 1. Organisms identical to those found in case 1 and in the blood of the patient in case 2 grew in these cultures. No other organism occurred.

Case 3.—In a white woman, aged 31, a sales-woman, a case of very mild degree occurred. There was a complaint of "rheumatic pains" about the knees. Other prodromal symptoms were absent. Four or five slightly painful nodes, from 1 to 2 cm. in diameter, developed in the anterior tibial surfaces. These nodes passed through the usual stages of involution characteristic of erythema nodosum. The patient continued at work. No fever or leukocytosis was observed.

A portion of cutaneous lesions was excised and planted as described in the preceding cases. Organisms having the same characteristics as those described grew in these cultures. No other organism occurred.

*Laboratory Data.*—Portions of the excised tissue from each of these cases were preserved in Zenker's fixative. Paraffin sections stained with hematoxylin-eosin showed the histologic characteristics of erythema nodosum. No features suggestive of tuberculosis were present. Sections were stained for acid-fast organisms. No such organisms were found in any of the cases. In each case, sections stained for bacteria by Gram's method showed pleomorphic organisms similar to those cultivated from the lesions. Coccoid forms, occurring singly and in pairs, predominated. Bacillary forms with bipolar granules and occasional club-shaped forms were present in smaller numbers. Numerous organisms were seen in the sections from case 2 (fig. 2). They were less numerous in sections from cases 1 and 3 (fig. 3), in which the disease was much less severe than in case 2. The organisms occurred both intracellularly and extracellularly. Many monocytes were seen with coccoid and rod-shaped forms within their cytoplasm. These organisms stained bluish black by Gram's method, and were easily distinguished from the brown pigment granules resulting from the destruction of erythrocytes.

## EXPERIMENTAL DATA

Animals were inoculated with recently isolated cultures. Twelve young, healthy rabbits, weighing from 800 to 1,200 Gm., and two healthy, half-grown guinea pigs were inoculated intravenously with fresh cultures of the strains obtained from each of the human beings in the cases reported. In some instances intravenous inoculation was combined with small subcutaneous and intramuscular inoculations. One rabbit showed no evidence of disease following such inoculation. Local lesions grossly and microscopically resembling those of erythema nodosum were found in each of the guinea-pigs and in eleven of the rabbits. The protocols of these experiments are similar in all essential details. To avoid repetition, two protocols will be given in detail, and the results of the remainder will be summarized.

*Experiment 1 (rabbit 145).*—The animal was a vigorous, active, half-grown white male weighing 1,150 Gm.

May 20, 1930: The sediment from 5 cc. of a twenty-four hour broth culture was injected into the marginal vein of one ear and 0.2 cc. of broth culture was injected beneath the skin of the other ear.

May 21: The sites into which inoculations were made, especially those extending above and below the point of intravenous injection, were bright red and slightly swollen.

May 23: The sites of injection were very red and moderately swollen and seemed hypersensitive. Otherwise the animal appeared normal. He was carefully wrapped in cloth and etherized under a bell jar to prevent bruising. In the skin over the back, shoulders and sides there were numerous areas of cutaneous hemorrhage. Some of them were solitary, being about 2 cm. in diameter; others occurred as groups of small hemorrhages from 3 to 5 mm. in diameter. One such area 5 mm. in diameter was present in the gluteal muscle and another in the skin

of the front leg near the wrist joint. There were numerous circumscribed congested spots, 3 mm. in diameter, in the lungs. The gallbladder was congested, and the bile contained blood. Otherwise all structures appeared normal.

The organism inoculated into the animal was recovered in cultures of sections from the gluteal muscles, from the bile and from the subcutaneous tissue of the ear.

In the following experiment the cutaneous lesions were observed for eight days, during which time they disappeared spontaneously. The animal was reinoculated and examined later.

*Experiment 2 (rabbit 146).*—The animal was a vigorous, active, half-grown white female, weighing 1,150 Gm., from the same litter as rabbit 145.

Fig. 4 (rabbit 146).—Area of infiltration adjacent to artery wall in ear. Numerous coccoid and a few bacillary forms are seen. This field was taken in an area corresponding to the square shown in figure 5. Zenker fixation, paraffin section; Gram stain; × 1,000.

May 20, 1930: The sediment from 5 cc. of a twenty-four hour broth culture was injected into the marginal vein of one ear, and 0.2 cc. of broth culture was injected beneath the skin of the other ear.

May 21: Along the inoculated marginal vein, extending 1.5 cm. above, and an equal distance below, the point at which the intravenous injection was made, there was an area of marked congestion 0.8 cm. in diameter and 0.4 cm. on either side of the vein. A circular area of congestion, 1.5 cm. in diameter, surrounded the point of the subcutaneous inoculation. These areas were swollen, bright red and apparently tender. The rabbit was less active than before and did not eat.

May 22: No apparent change occurred in the conditions noted.

May 24: The areas described had not extended; they had become deep red and were still swollen.

May 26: The redness and swelling had decreased somewhat.

May 28: The areas described were light brown. No swelling was perceptible. The rabbit behaved normally. The sediment from 10 cc. of a twenty-four hour broth culture was injected intravenously and 0.2 cc. of broth culture was injected under the skin of the ear. Two similar injections were made into the gluteal muscles.

May 29: Zones of marked congestion and moderate swelling extended along the vein injected, and surrounded the point of subcutaneous inoculation.

May 31: The animal appeared ill. The areas of congestion had become deep red.

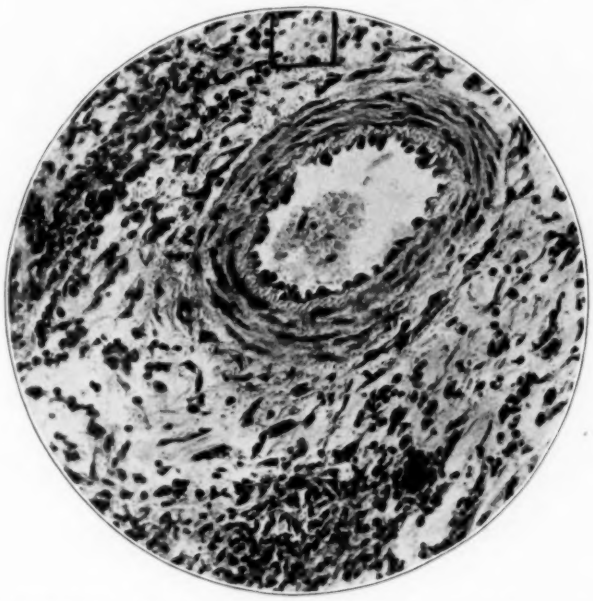

Fig. 5 (rabbit 146).—Periarteritis in ear. Note edema and mononuclear infiltration. This lesion is in an advanced stage. A corresponding section of this tissue, stained by Gram's method, showed many organisms in the perivascular area (fig. 4). Zenker fixation, paraffin section; hematoxylin-eosin stain; × 230.

The rabbit was wrapped in cloth to prevent bruising and was etherized under a bell jar. A reddened erythematous area 0.7 cm. by 2 cm. extended along the marginal vein of the ear. A similar area 1.5 cm. in diameter surrounded the site of subcutaneous inoculation in the ear. In the gluteal muscles at the sites of inoculation there were two oval areas 0.7 cm. by 1.5 cm. in size. These areas were reddened and erythematous, and the muscle fibers appeared opaque. No other muscular or cutaneous lesions were seen. The heart appeared normal. The lungs contained scattered circumscribed areas 0.5 cm. in diameter. These areas were deep red and did not collapse readily. No other abnormalities were seen.

The organism inoculated was recovered in cultures from the lesions in the gluteal muscle and from the cutaneous lesion on the ear.

HISTOLOGY IN EXPERIMENTAL ERYTHEMA NODOSUM

Histologic examination was made of the cutaneous, muscular and pulmonary lesions. The subcutaneous tissue of the ear contained localized areas of edema (fig. 6) in which the capillaries and veins were distended and in which there were numerous red cells outside the vessels. Numerous mononuclear cells and a few leukocytes were present. About the arterioles these changes were characteristically perivascular in distribution, (fig. 5) and extended as a sheath along the vessels. In sections stained by Gram's method pleomorphic bacilli and coccoid

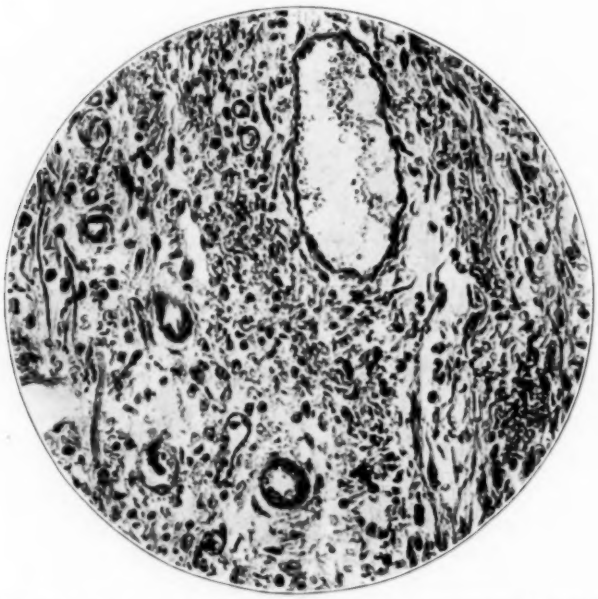

Fig. 6 (rabbit 145).—Periphlebitis of ear. Note extravasated red cells, edema and endothelial swelling in the small vessels. This lesion is of three days' duration; × 230.

forms were seen in the infiltrated areas about the vessel walls (fig. 4). These forms were exactly similar to those seen in the sections from human beings and to the organisms cultivated in such cases.

The lesions in the skeletal muscles contained necrotic muscle fibers about which there were capillary engorgement, extravascular red cells and numerous monocytes. There was no tendency to suppuration (fig. 9).

The small circumscribed congested areas in the lungs showed marked dilatation of capillaries and moderate capillary hemorrhage. There was peribronchial mononuclear infiltration.

In the kidney of rabbit 145 there were scattered areas of congestion and capillary hemorrhage.

In the two guinea-pigs and in eleven of the twelve rabbits erythematous cutaneous lesions were produced. In one rabbit there were

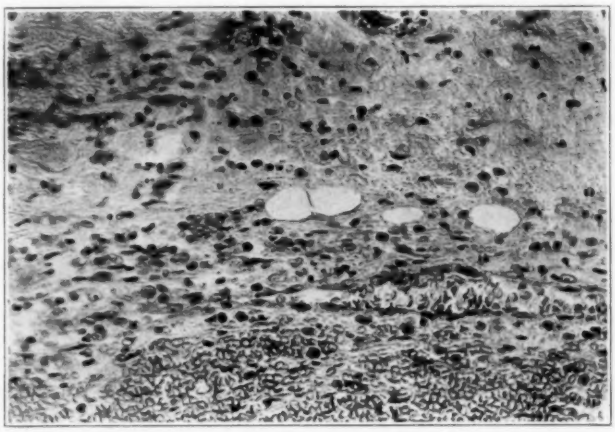

Fig. 7 (rabbit 126).—Subcutaneous lesion. Note edema, extravasation of red cells and monocytic infiltration. A few polymorphonuclear cells are present; × 230.

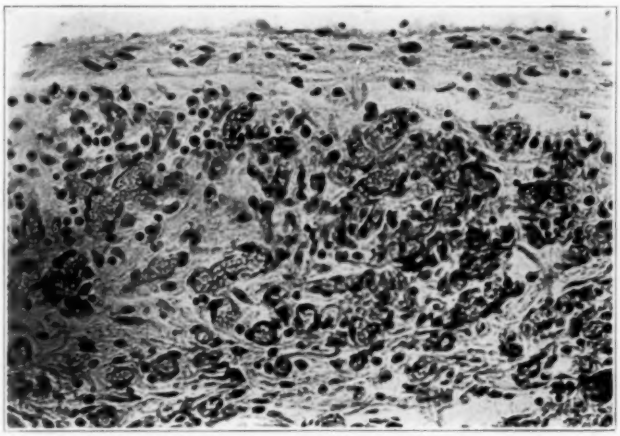

Fig. 8 (rabbit 113).—Lesion in subcutaneous fascia. Note the dilatation of vessels, erythrocytic and monocytic infiltration and edema; × 230.

extensive hemorrhages, purpuric in character, involving the muscles of the back, the chest and the limbs. In each case the histologic features of the lesions were similar to those described for rabbits 145 and 146. In five animals there were such lesions in the kidneys; in six, in the lungs;

in eight, in the muscles; in one, in the periosteum of the femur, and in one, in the gallbladder.

The essential features common to all of these lesions were dilatation of the veins and capillaries, perivascular edema and infiltration of monocytes and lymphocytes and extravasation of red cells from the capillaries. These are the essential histologic features present in the lesions of erythema nodosum in man. In animals these lesions were found in muscular, renal and pulmonary locations as well as in cutaneous and subcutaneous tissues. Lesions in these areas have not been seen in man, though symptoms referable to the muscles, kidneys and lungs have been noted frequently.

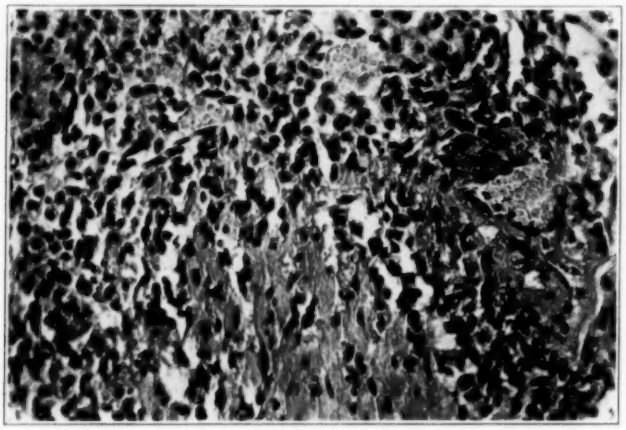

Fig. 9 (rabbit 111).—Lesion in gluteal muscle, showing extravasation of red cells and marked monocytic infiltration; × 230.

### CONTROLS

Bits of skin and subcutaneous tissue were obtained during aseptic surgical operations on various parts of the body in conditions other than erythema nodosum. Five such sections of normal subcutaneous tissue were cultured by the technic described. In four of them all the cultures remained sterile. In one a strain of Staphylococcus albus grew. No other organism occurred in these cultures. The Corynebacterium found in erythema nodosum apparently is not normally found in the deep tissue of the human skin.

Four young healthy rabbits were similarly inoculated with a culture from Corynebacterium lymphophilum recently isolated from lymph nodes in a case of Hodgkin's disease. In none of these rabbits were there recognizable lesions of any kind. In animal pathogenicity the Corynebacterium isolated from erythema nodosum differs markedly from Corynebacterium lymphophilum.

SUMMARY

The view that erythema nodosum is an acute infectious disease is held by many observers. The clinical manifestations in all of the cases we have seen support this view.

An organism of the genus Corynebacterium was cultivated from the subcutaneous tissue in each of three cases of erythema nodosum. This organism was also cultivated from the blood in one case of unusual severity. In thirteen of fourteen inoculated animals lesions were produced that had the histologic characteristics of those of erythema nodosum. The same organism was recovered in cultures from these lesions. Similar organisms were demonstrated in sections from lesions in human beings, and in the lesions in the inoculated animals. These observations indicate that erythema nodosum is a specific infection of which the organism described is the probable cause.

It is probable that the organism found in these cases is identical with that described by Rosenow. It is not identical with any species listed by the Society of American Bacteriologists. If these observations are to be confirmed, this species should be given appropriate designation. The term Corynebacterium cutis-nodosae is suggested.

# TREATMENT OF VASCULAR NEVI BY INJECTION OF SCLEROSING SOLUTIONS

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AND
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This work has been undertaken with the hope of offering a more effective method of treatment for vascular nevi. Although present methods of treatment by radiation, electrocoagulation and excision have been more or less successful, no one of them has been entirely satisfactory. In an effort to avoid operations, scars, undue expense or the possibility of recurrences entailed by the usual methods, we have employed the modern sclerosing agents used in the treatment for varicose veins, injecting these solutions into the vascular nevi in minute amounts.

The following technic has proved the most desirable in order to avoid scarring, sloughing and pain. Hemostasis, although not absolutely essential, is nevertheless advisable and usually can be obtained in superficial angiomas by the use of McPheeter's malleable varicose vein occluder. Ordinary sterile precautions are observed. The area under treatment is painted with tincture of iodine and alcohol. The only equipment necessary is a small syringe, tuberculin or 5 cc. Luer, with a 25 gage hypodermic needle, preferably of platinum. The small needle enters the lesion easily with the least possible tearing, resulting in minimum bleeding or loss of solution on withdrawal. The solutions used were 20 per cent quinine-ethyl carbamate or sodium chloride and 50 per cent dextrose. All proved equally efficacious. During the early stages of our work these solutions were diluted up to one part of the solution in six of water. However, as the work progressed we noted that we were able to use, with constant safety, dilutions of one part of the solution in three of water, and in some instances one part of the solution in two of water.

The amounts injected into each lesion were no more than 2 minims (0.12 cc.) in any one area, the number of areas injected varying with the size of the lesion. Each injection blanched a circular area extending about 8 mm. around the point where the needle was introduced.

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When the vessels were directly entered, the effect extended a little further and the vessels, which were previously indistinguishable, one after another were seen to whiten. A margin of 5 mm. about the blanched area caused by each injection should be left untreated for the sake of safety. The depth of the injections depends on the depth of the nevus, the object being to distribute the sclerosing fluid throughout the deeper parts of the angioma. Thus, after introducing the needle and injecting a minute amount, the needle is advanced a little and another small injection is made, and so on, until the 2 minims are used. We had one adult patient who was apparently hypersensitive to quinine and who developed severe palpitation of the heart and ringing of the ears after the first injection of quinine-ethyl carbamate solution. Bearing

Fig. 1.—M. B., aged 3 months, with cavernous hemangioma of the right labia majora, 2 by 2 cm. before treatment.

in mind similar possibilities in infants, we feel that the first injection should be limited to one area with no more than 2 minims if this solution is used. However, in one adult patient who had a cavernous hemangioma we used as much as 2 cc. of full strength quinine-ethyl carbamate solution in one injection with good results.

The blood vessels composing the lesion were entered wherever possible, but we discovered that this was not essential to the sclerosing of the lesions because perivascular injections also effectively closed the delicate blood vessels. After the injection, if bleeding was present it was controlled by gentle pressure.

In our experience, injections should not be given oftener than at weekly intervals. The major complications to be avoided are slough-

ing and scarring. Pain was almost entirely eliminated because of the minute amounts injected. Following each of the first two injections the patients usually complained of moderate tenderness and swelling of the lesion. However, this condition disappeared within twenty-four hours and did not occur following subsequent injections.

We have treated twenty patients with vascular nevi by this method. No attempt was made in carrying out the work to limit ourselves to any particular type, the lesions treated having included cavernous and capillary nevi, as well as in three instances port-wine marks; nor has the location, size, age, state of the lesions from previous treatment or the age of the patient influenced the results. The cavernous type has shown the most immediate and gratifying response, frequently com-

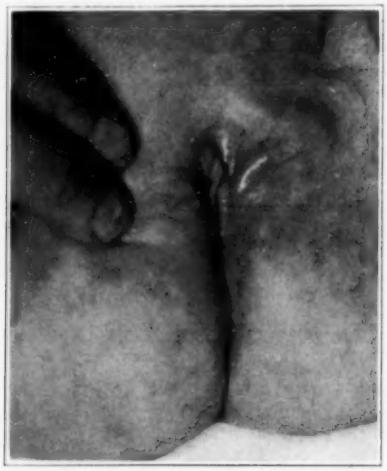

Fig. 2.—Same patient, two and one-half months later, after six injections of solution of quinine-ethyl carbamate diluted 1:2; an average of five areas was injected with 2 minims at each treatment. Each cubic centimeter of the solution used contains quinine hydrochloride, 0.133 Gm., and ethyl carbamate, 0.066 Gm., before dilution.

pletely involuting after three or four weekly injections. The strawberry type has also responded well. Port-wine marks have been much more recalcitrant, but in three cases the improvement, although meager, has been accompanied by no scarring and has warranted a continuance of this form of treatment.

The injection of the modern sclerosing agents used in varicose vein therapy is a useful method of eradicating vascular nevi. Sloughing, scarring and pain can be avoided by careful technic. This method is particularly valuable because of its effectiveness, simplicity and low cost.

# VERRUCAE VULGARES (PALMAR AND PLANTAR)

## TREATMENT BY INTRAMUSCULAR INJECTIONS OF BISMUTH SALICYLATE

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Numerous remedies have been employed in the treatment of common warts, ranging all the way from magic charms to surgical excision. Destruction by acids, electricity, carbon dioxide snow and radium, etc., have all produced good results in many cases.

When large numbers of warts are present, however, local destructive measures are tedious, painful and, in the case of children, frequently difficult to carry out.

Intramuscular injections of sulpharsphenamine have been used with success by some physicians, but the results are often disappointing, and the drug is not free from danger in such ailments as common warts. Since the administration of mercury by mouth is frequently beneficial in the treatment for juvenile flat warts, it was thought worth while to test the effect of another drug, bismuth, which in syphilis at least has a therapeutic effect similar to that of mercury.

Previous experimental work has proved that warts are infectious and are apparently due to a filtrable virus. It is conceivable that in some cases warts may be due to an allergic state, certain parts of the body responding sympathetically through the blood stream, as in the case of fungus infections.

Microscopically, there is no proof of this theory, but the frequent symmetrical localization of verrucae on the hands or feet, or both, as is often seen in fungus infections, suggests such a possibility.

Altogether forty-nine patients have been treated by intramuscular injections of bismuth salicylate; five were adults, and the others, children. Thirty-four of these patients were observed for varying periods following treatment, and in all cases the warts completely disappeared.

The injections were given one week apart; they were administered intramuscularly into the upper outer gluteal quadrant, the amount injected varying according to the age. Children from 6 to 10 years of age were given 1 grain (0.065 Gm.) of bismuth salicylate intra-

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muscularly; children from 10 to 13 years of age, 1½ grains (0.0974 Gm.), and the older ones, 2 grains (0.13 Gm.).

Recently the technic has been changed as follows: one injection is given, and the wart is observed. Regression usually begins immediately, and no further treatment is given until the condition becomes stationary. Subsequent injections are then administered, sometimes with an interval of two or three weeks between treatments.

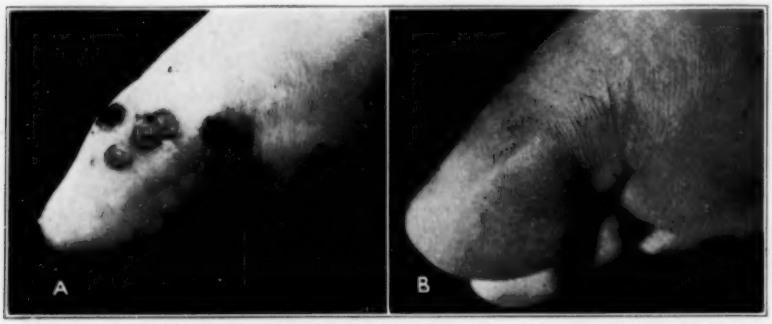


Fig. 1.—*A* shows a condition of one year's duration. *B* shows the same area after two treatments.

Fig. 2.—*A* shows a condition of four months' duration. *B* shows the complete disappearance of warts after one treatment.

An interesting peculiarity was observed; the plantar warts, so-called papillomas, respond spectacularly to this treatment; in many cases more rapidly than those on the hands.

In some cases, the warts seem to melt; in other cases, the wart comes out like a kernel; but in general, layer by layer disappears, beneath which bloody points (projections of the papillae corii) occur which gradually dry up and come off, leaving a smooth area without

scars. The pains and aches become less intense after the first injection. Sometimes one and sometimes three injections are sufficient treatment for warts that have been annoying for months. The largest number of injections given was nine; this number was given in only one case.

## REPORT OF CASES

CASE 1.—A. W., a boy, 12 years of age, on May 27, 1930, presented eighty-six warts on both hands, some of which were the size of a large pea; their duration was indefinite.

Intramuscular injections of bismuth salicylate were given one week apart in a dosage of 1½ grains. After the first treatment, the warts became flatter and showed a tendency to become looser. After the second injection the warts continued to regress in the same way; the smaller warts showed numerous bloody points, and after the third injection some of the small warts came off. Three more injections were given, and after the fifth, only fifty-four warts remained. The condition of the hands was greatly improved, and the skin appeared smooth at the site of the previous warts, without scarring. The patient has not been seen since this treatment; efforts to locate him were in vain, but a school nurse reported that he was well.

CASE 2.—M. K., a girl, 12 years of age, on May 26, 1931, presented a group of eight plantar warts the size of a pea on the great toe of the right foot and one wart on the ball of the left foot, of the same size. The duration was one year, and the warts were very painful. Bismuth salicylate was administered in a dosage of 1½ grains; the second injection was given on June 11, according to the new technic. When the patient was next seen, on October 24, a second photograph was taken to show the results obtained after two treatments.

CASE 3.—J. D., a girl 11 years old, on June 4, 1931, presented two warts on the right palm; one was the size of a large pea, the other, the size of a match head. They were very annoying when she was working. An injection of 1½ grains of bismuth salicylate was given intramuscularly on the day of presentation. One week later, the patient showed spectacular improvement; no more treatment was given, and two weeks later the warts had entirely disappeared.

The photographs taken before and after treatment by intramuscular injections of bismuth salicylate represent the results obtained in a few cases.

## SUMMARY

1. A new method of treatment for plantar and palmar warts (verrucae vulgares) by intramuscular injections of bismuth salicylate is described.

2. Thirty-four cases followed up in which this treatment was given showed cure, and no relapses were seen one year after treatment.

3. The method is simple and inexpensive, and the results of treatment are prompt.

4. Warts located about the nails were the most resistant; those on the hands were less resistant, and those on the feet responded most rapidly.

# TWISTED HAIRS (PILI TORTI)

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The anomalies of development of the hair (loose hair, moniliform hair, pinsel hair, breaking nodular hair, bayonet hair, atrophy of the ends of the hair, knotted and pseudoknotted hair) are characterized by hairs of irregular shape, which are more or less short and thin; in general, dry and brittle, and break at the slightest provocation out of the follicle or along the shaft. A symptom common to all is the fragility. The patients show a peculiar appearance, varying from complete baldness to a straight and frizzy-haired scalp.

A patient in the last group recently came under my observation. The hairs were thin and brittle, but a peculiar feature was the twisting of the shaft on its own axis, in some sections with very narrow twists, in others with large twists, occurring at almost regular intervals and involving the entire scalp.

Very little can be found in the literature on twisting of the hair, either as an anomaly of few hairs, or as a disease of the entire scalp. For this reason I think that the following case is worthy of publication.

## REPORT OF A CASE [1]

*History.*—A. B., a girl, aged 7 years, born in Rhode Island, of Italian descent, was brought to the Skin Out Patient Department of the Rhode Island Hospital on April 20, 1931, because of a large area of scanty and short hairs on the occiput, which had existed since birth.

She was the youngest of eight children, four boys and four girls. She looked like a normally developed child physically. The first teeth appeared when she was 6 months old, and she began to walk at 10 months, before the other children. Her intelligence was slightly below normal. She had always enjoyed good health.

The mother said that there was no history of sickness in the family. In regard to the scalp, the mother said that she had never noticed or heard of any abnormality in other members of her family; no information could be obtained regarding the paternal side.

*Examination.*—A general physical examination showed no apparent abnormalities in the different systems, particularly in the endocrine glands. Roentgen examinations of the sella turcica and the rest of the body also gave negative results.

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From the Department of Dermatology and Syphilology of the Rhode Island Hospital.

1. This patient was presented at the quarterly meeting of the New England Dermatological Society, Boston, Oct. 14, 1931.

The teeth were poor and slightly notched, with spaces between them. The tonsils were enlarged. The finger-nails and toe-nails were normal.

Scalp: The hairs were a dull blonde color, lank and frizzy, with a wild, bushy appearance. They had never been cut, but broke spontaneously or on slight injury, at different lengths, from 1 to 4 cm. in the occiput to 10 to 12 cm. in the parietal region, the latter being the maximum length they could reach (fig. 1).

The hairs were thin, dry, straight and moderately entwined, and the patient objected to having them plucked, as a normal child would; the mother said that the girl always complained when the hair was combed.

On close examination with the naked eye or with a magnification lens on a dark field, it was easy to see sharp twists in the hair, of different breadth and number, occurring at fairly regular intervals and refracting the light.

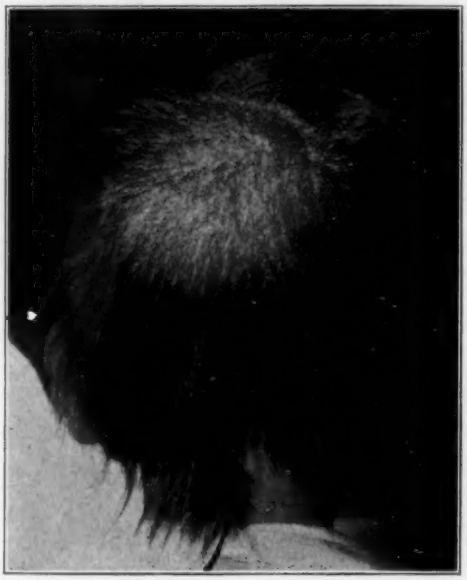

Fig. 1.—Back view of the lank and frizzy scalp, showing the area of partial alopecia.

The hairs on the occiput were short, thin and almost colorless, and were more fragile than the hairs on the rest of the scalp. The bulb was thin and coiled (fig. 2). The shaft, at the beginning, was apparently round or slightly flattened. Shortly afterward, without a great change of the flattening index, the shaft twisted suddenly on its own axis, making groups of five or ten twists, as narrow as about 0.4 mm. each. Beyond these twists followed longer twists, and the hair broke about from 1 to 4 cm. from the follicle. Along the shaft could be seen several points of fracture, some initial, some pinsel or broom-shaped, as in cases of nodular breaking of the hair. The breaks occurred in various parts of the shaft, independent of the narrowness or the number of the twists.

The hairs of the rest of the scalp had more color and more resistance, so that they broke only when about from 10 to 12 cm. in length. The bulb was larger and less coiled than on the occiput. The shaft appeared stronger and, at the beginning, fairly cylindric or elliptic; then it changed quickly into a flattening of

very low index and twisted with long turns. Among the series of long turns there were some isolated, very narrow ones, making a complete twist almost in the same place. At almost regular intervals there were groups of five or ten twists as narrow as in the hairs of the occiput, of from 0.4 to 0.9 mm., to several millimeters in length. The twists seemed to run always in the same direction, and no evidence of inversion was noticed. Some hairs appeared straight and normal

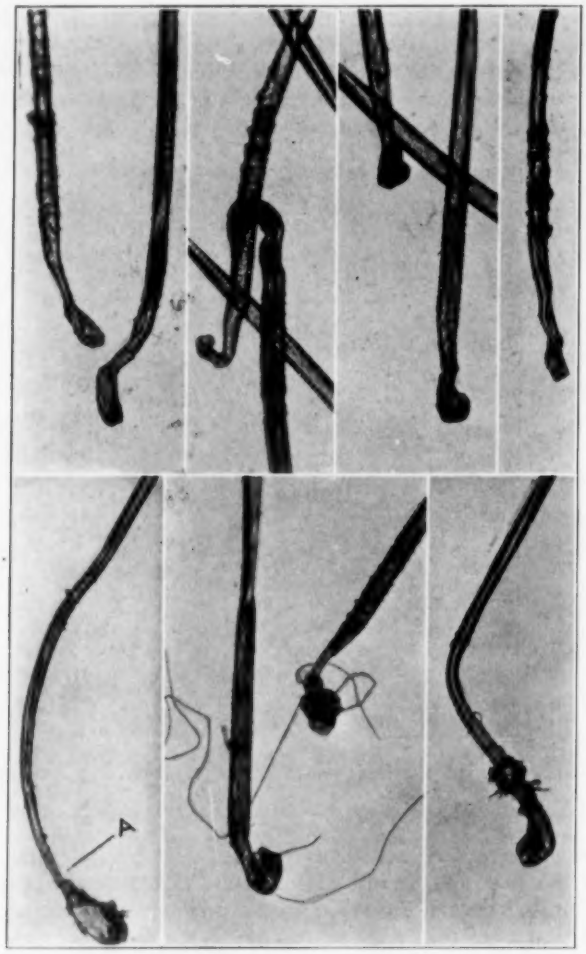


Fig. 2.—Different kinds of roots, some coiled, some twisted and some spoon-like, and an eyebrow hair (*A*) with a sharp and narrow turn at the beginning of the shaft; reduced from a magnification of about × 40.

for a long portion of their length. Some were colorless, thin, from one-third to one-fifth the diameter of the others, and straight. Some, grouped in the same follicle or adjoined to a hair of normal size, were atrophic, filiform, flattened and twisted. In general, no distinction was appreciable between the cortex and the medulla.

Almost all of the twisted hairs were flattened to a very low index, but not much difference in the degree of flattening was noticeable in the narrow and the large twists. Narrow twists were observed in sections that were almost cylindric, as in the sections from the eyebrows (fig. 2 *A*).

Eyebrows: The eyebrows were very scanty, thin, fragile and poorly colored, showing twists refracting the light to the naked eye. At the follicle, the shaft,

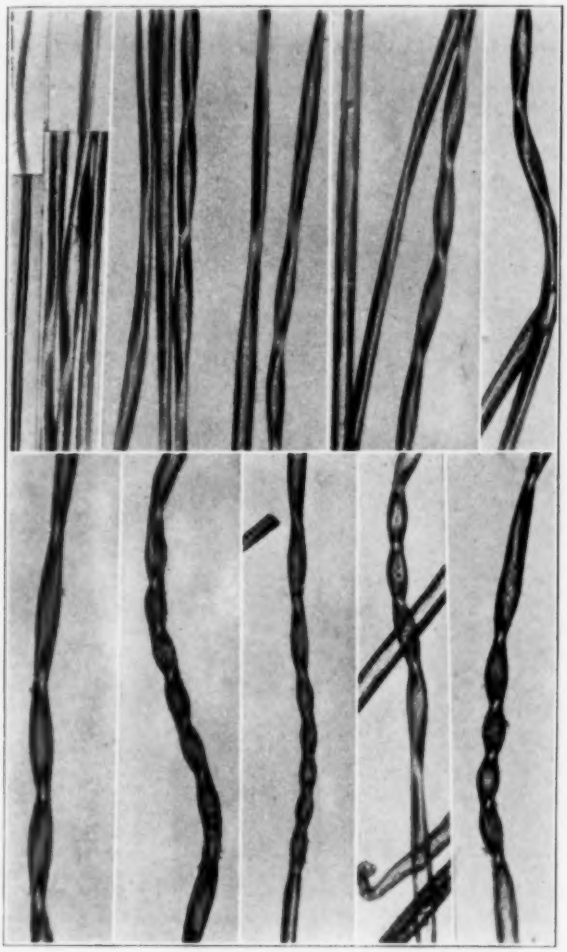

Fig. 3.—Hairs of various size, color, degree and kind of twisting; reduced from a magnification of about × 40.

of a fairly cylindric shape, made a sharp, narrow, complete twist and continued slightly flattened with a few long and narrow twists, but never so narrow and grouped as in the other hairs previously described (fig. 2 *A*).

Eyelashes: The upper row of eyelashes was normal in number, shape and color. In the lower row, the eyelashes were scanty as a consequence of chronic blepharitis.

The appearance of the hairs did not change with the season, the weather or other conditions.

The lanugo hairs of the rest of the body were apparently normal in shape and distribution.

The skin of the scalp was rough. A sharp keratosis pilaris was noticeable on the knees, legs and, in a minor degree, the rest of the body.

*Laboratory Findings.*—The urine was normal. Examination of the blood showed: urea nitrogen, 13 mg. per cubic centimeter; sugar, 103 mg.; red cells, 4,800,000; white cells, 9,600; hemoglobin, 78 per cent. A differential count showed:

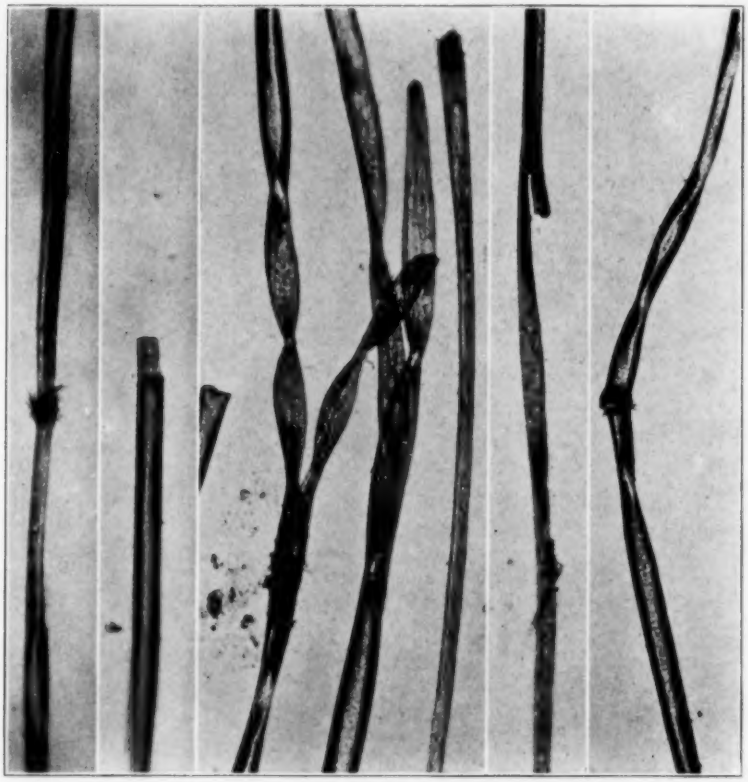

Fig. 4.—The splitting and breaking of the hair by stretching or at a slight provocation; about × 40.

polymorphonuclears, 58 per cent; lymphocytes, 38 per cent; eosinophils, 4 per cent. The Wassermann and Hinton reactions were negative. The average basal metabolic rate was plus 12. Examination and culture of the hairs showed them to be negative for hyphomycetes and bacteria.

The resistance of the hair to stretching was as follows: The maximum weight the hairs could support was from 20 to 30 Gm., whereas a normal hair from a patient of the same age can support a weight of from 70 to 90 Gm. The elasticity, measured by stretching, showed that the hair could increase approximately one seventh of its length, whereas the increase in length of a normal hair is from one fifth to one third.

The hairs generally broke by splitting (trichoptilosis). The shaft opened longitudinally in the direction of the larger and longer diameter, making two ribbon-like halves, as shown in figure 4. The end of the broken hair soon became broomlike, as in trichorrhexis nodosa.

The hair observed in cedar wood oil appeared transparent and uniform, with enlargements and constrictions, the latter corresponding to the most narrow turns. The ensemble, at a superficial observation, resembled some pictures of monilethrix. In cedar wood oil the points of fracture were demonstrated clearly, some of which

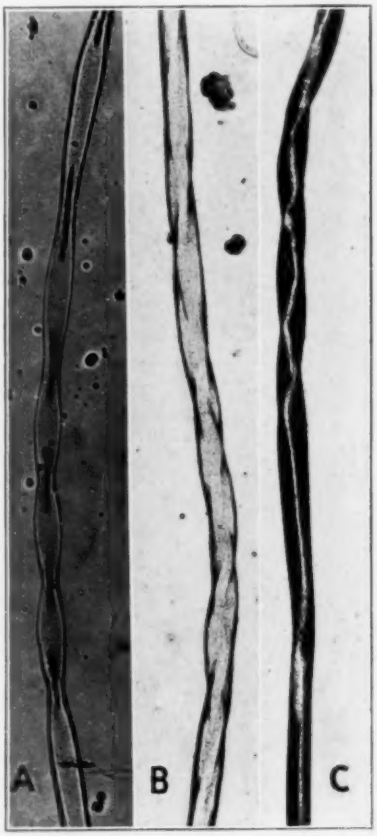


Fig. 5.—*A* shows points of fracture corresponding to the most narrow turns, in cedar wood oil; *B*, a hair in glycerin with compound turns, of a quadrangular shape in cross-section; *C*, a hair in glycerin with uninterrupted medulla; about × 40.

were strictly related to the turns of the shaft under the pressure of the cover glass, and some of which were scattered along straight sections of the shaft (fig. 5 *A*).

The hair immersed in glycerin showed the cuticular scales of imbricate type and, fairly well, the medulla. In some hairs the medulla was visible without interruption all along the shaft (fig. 5 *C*).

Immersion in a caustic solution (a weak solution of potassium hydroxide, 10 per cent of sodium or potassium sulphide) showed a sharp difference from normal hair under the same conditions of age and color. In a few seconds, one of the patient's hairs swelled (fig. 6), showed the swollen tapeworm-like cortex and the medulla, and, in a few more seconds, became uniform, the different parts being no longer distinguishable from each other, and it burst in several points.

A normal hair took a much longer time to swell, and after from about five to ten minutes it still allowed differentiation of the cortex from the medulla. Later it became the same size as the patient's hair, and of similar appearance.

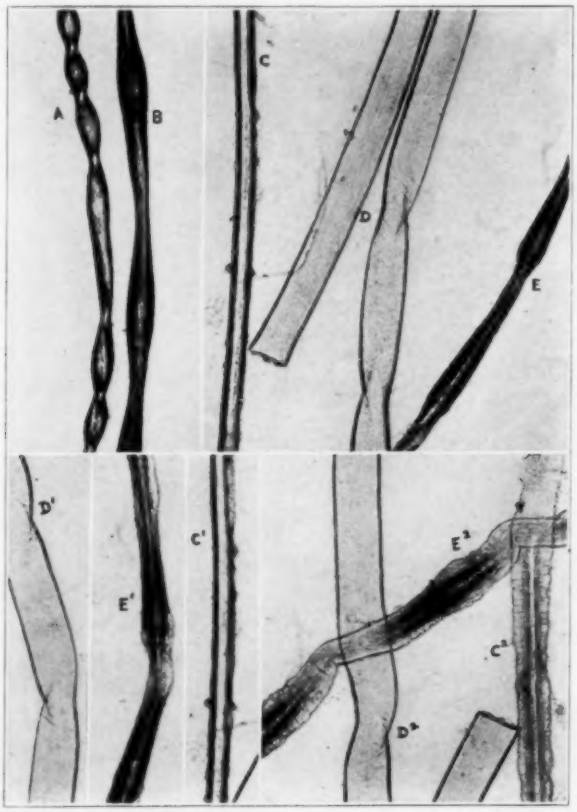


Fig. 6.—*A* indicates an untreated twisted hair; *B*, an untreated moniliform hair; *C*, a normal hair; *D*, a twisted hair; *E*, a moniliform hair, after one minute's immersion in 10 per cent sodium sulphide, showing the quick swelling of the twisted hair and the slow swelling of the others; $C^1$, $D^1$ and $E^1$, the same hairs after two minutes; $C^2$, $D^2$ and $E^2$, the same hairs after four minutes. The normal hair still allows differentiation of the cortex from the medulla; reduced from a magnification of about × 40.

*Biopsy.*—Two small pieces of skin were removed with a punch from two distant points of the occiput, fixed in Zenker's fluid and stained with hematoxylin-eosin. The horny layer was thickened, and some of the openings of the follicles were

blocked by keratotic plugs. In those follicles a slight twisting of the hair was observed. No inflammatory changes were noticeable, except for a few small lymphocytic groups around some vessels. The sebaceous glands, in one of the two sections, were fairly normal. In the other section, they showed marked atrophy, and, in places, they were completely absent.

At several points two or more thin hairs were contained in the same follicle. One follicle had seven hairs. The groups were, in general, of atrophic, filiform hairs, but also hairs of normal size were observed in groups of two or more.

The hairs cut in cross-section within the follicle were round and showed different diameters, from a fairly normal to a very small one. Similar pictures observed in sections of the scalp in cases of monilethrix were considered by some authors as sections cut through the constriction of the hair shaft. In my

Fig. 7.—Serial sections through a twisted follicle; reduced from a magnification of about × 100.

case, as probably in the cases of monilethrix, they were simply cross-sections of atrophic hairs.

Bunches of hairs cut in cross-section showed a moderate degree of flattening and, in general, were oval. Some sections were irregularly triangular or quadrangular, owing to the passage of the knife through the most narrow and grouped twists (see fig. 5 *B*, of a hair apparently quadrangular).

## COMMENT

Danforth,[2] in a remarkable study of the hair, is the only author, as far as I know, who paid attention to and gave a most detailed description

2. Danforth, C. H.: Studies on Hair: With Special Reference to Hypertrichosis, Arch. Dermat. & Syph. **12**:76 (July) 1925.

of the anatomy and physiology of twisting of the hair. He related this condition to a flattened shaft, and said that:

> This twisting varies greatly in different hairs, being almost absent in some cases and pronounced in others. It may occur in hairs that have the superficial appearance of being lank and straight.

Further:

> Generally the twisting consists of a series of half turns so that one side of the hair is alternately toward the observer and away from him. The length of hair that is involved in the twists ranges from less than a millimeter to several millimeters, or so great a distance that it is difficult to detect any twist at all. In general the twisting is not continuous but interrupted. When the twists or half turns involve only a short distance on the hair shaft, and especially when two or more twists occur close together, the hair tends to change its direction in a way that gives it a peculiar frizzy character. Since this apparently irreversible twisting of the hair on its own axis may be seen even within the follicle, there is some probability that it is determined there, perhaps by irregular or periodic changes in the function of the papilla, or by irregular compression of the sheath immediately above.
>
> Strangely, this characteristic has been as much neglected in hair work as some of the other traits have been emphasized.

Textbooks on anatomy, physiology and dermatology, although published after Danforth's paper,[3] do not mention the normal slight twisting of the hair shaft on its own axis, which is a common observation. Careful papers, on the results of studies of hundreds of scalps, do not mention this subject, except as a feature of secondary importance in pseudoknotted hairs,[4] in piedra due to the weight of the material accumulated around the hair shaft and in monilethrix due to the weakness of the hair at the point of constriction.

Danforth goes a little too far if he considers as normal a "lank, straight, frizzy" haired scalp and hairs having grouped twists "of less than a millimeter of length." A pronounced twisting of the hair is a very rare occurrence, and this is the reason why it "has been so much neglected" by investigators.

The case published by Freund,[5] under the title "A Hitherto Undescribed Condition of the Hair," is the only observation, as far as I know, fairly similar to the present one. It was the case of a girl, 2

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3. Jadassohn, J.: Handbuch der Haut- und Geschlechtskrankheiten, Berlin, Julius Springer, 1927. Hubbard, S. D.: A Treatise on Diseases of the Hair and Scalp, Philadelphia, Lea & Febiger, 1928. Pinkus, F.: Die Einwirkung von Krankheiten auf das Kopfhaar des Menschen, Berlin, S. Karger, 1928. Glaister, J., Jr.: A Study of Hairs and Wools, Egyptian University, Cairo, Egypt, Misr. Press, 1931.

4. Kren, quoted by Danforth (footnote 2).

5. Freund, E.: Su un'anomalia congenita dei capelli finora non descritta, Gior. ital. di dermat. e sif. **66**:514 (April) 1925.

years old, with brittle and frizzy hairs, which were flattened and twisted, but which had large turns and not the narrow and grouped turns of the hairs of my patient. The eyebrows were scanty and twisted. In cross-section, the hairs were oval. The pathogenesis was obscure.

Freund [5] quoted the case (not published), reported in brief and without details at a dermatologic meeting in Germany by Riecke, of a girl, aged 8 years, with ribbon-like, twisted hairs, which was called "trichokinesis."

These cases should be included in the group with fragile hairs (fragilitas crinium), on account of the common symptom, the fragility. However, as three cases have already been reported and as the anomaly in my case is so pronounced as to make it almost unique, I think that they should have a name taken from the most striking feature and be called: twisted hairs (pili torti-trichotortosis).

In regard to the differential diagnosis, I think it unnecessary to recall the characteristics of the various types of fragile hairs mentioned to demonstrate that none of them will fit in with the picture of the present malformation.

## PATHOGENESIS

The pathogenesis is obscure. The disease is congenital. In my case no information could be obtained on the paternal side, and on the maternal side the history showed no abnormalities; so it can be assumed that the disease came through the father.

One may think of the disorder as a disturbance of the endocrine system, but no data have been found to support this view. The slight malformation of the teeth is not sufficient for a diagnosis of congenital syphilis. As with other anomalies, particularly the moniliform hair, which has been the most carefully investigated, various explanations have been advanced, but all remain in the field of hypotheses.

The impaired secretion of the sebum is certainly responsible for the dryness and the brittleness of the hair. The compression within the follicle and above the follicle by keratotic plugs might be the cause of the flattening and the twisting of the hair shaft within the follicle and after it emerges. However, other dyskeratoses (keratosis pilaris, lichen spinulosus, trichostasis nodosa, etc.[6]) show evidence of plugging of the follicle by layers of horny tissue and of coiled and wrapped hair shaft within the follicle, and no subsequent twisting of the hair has been noticed.

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6. Vignolo-Lutati, C.: Trichostasis nodosa atrophicans barbae, Gior. ital. d. mal. ven. **57**:272, 1916. Freund, E.: Contributo allo studio della keratosi spinulosa (lichen pilaris seu spinulosus Crocker), ibid. **64**:1195, 1923 (plate V, fig. 4).

It is also difficult to explain why, if the flattening of the hair is the cause of the curling, knotting and twisting, one finds twisted hairs with a very high index of flattening (the hairs were almost cylindric), and why the curling is a common occurrence and the twisting and knotting are rare.

The fractured hair ends in a broomlike formation, as has been observed in other fragile hairs (trichorrhexis nodosa, etc.), or is divided into two ribbon-like twisted halves. It is clear that in the malformations, as well as in my case, the essential fact is the fragility of the hair, and that the broomlike end, the broomlike nodules or the split hair are merely traumatic formations in a fragile hair.

The quick swelling and bursting after immersion in a caustic solution seem to be symptomatic of a fragile hair.

I have but few cases to substantiate this idea. The hairs of Freund's patient showed a time of swelling about the same as the hairs of mine. Exactly as with the hairs of my patient was the result with: the white hairs of a man 90 years old; the coarse hairs of an old woman, apparently normal, with split and broomlike ends; the coarse hairs from an arm in a case of marked keratosis pilaris and psoriasis; the split ends and the portions of hairs injured by mechanical waving and curling, whereas the rest of the hair responded as a normal one. In two cases in which there were thin hairs which had been bleached with peroxide, the hairs showed an almost instantaneous swelling and a very rapid disintegration, easily demonstrable at the point of passage between the treated and untreated part of the hair. On the contrary, in a typical case of moniliform hair (typical for shape, but coarse, not breaking out of the follicles and involving only part of the hairy scalp), the hairs showed a resistance as great as a normal hair (fig. 6).

The hairs in cases of alopecia areata, favus, seborrheic dermatitis, ichthyosis, defluvium capillorum, chronic eczema and those regrowing after roentgen epilation, etc., show the same resistance as do normal hairs.

The multiplicity and grouping of atrophic hairs in the same follicle (comparable to similar abnormalities of the teeth) appear as unusual features, possibly due to a retarded or abnormal development and related to the subsequent fragility of the hair.

The partial alopecia of the occiput is evidently due to a more severe degree of fragility of the hair in that section of the scalp together with the friction on the pillow. The scantiness of the eyebrows might be due to the same two causes.

## TREATMENT AND PROGNOSIS

Treatment for the anomalies of development of the hair is in general unsatisfactory. Some investigators reported good results with the

x-rays in cases of monilethrix. On those premises, the patient in the case reported was given an epilatory dose on a small area of the occiput with the intention of epilating the entire scalp in case of success; however, no epilation was obtained.

In the meantime, hydrous wool fat was gently rubbed on the scalp, and after two months of this treatment, a sensible improvement was noticeable in the strength and number of hairs on the occiput and in the appearance of the entire scalp. This gives some hope of a favorable outcome.

## SUMMARY

An almost unique case of congenital malformation of the hair has been reported, characterized by hairs fragile and sharply twisted on their own axes, making an ensemble of a lank and bushy scalp and a partial alopecia.

The case is the third recorded in the literature, and is the most pronounced one. It has been called: twisted hairs (pili torti-trichotortosis).

The pathogenesis is obscure.

Dr. B. E. Clarke, pathologist of the Rhode Island Hospital, made the photomicrographs used in this article.

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# CUTANEOUS MELANOMAS

## WITH SPECIAL REFERENCE TO PROGNOSIS

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MILWAUKEE

Veterinarians were the first to describe melanomas, as occurring in horses, in 1784. Dupuytren [1] is credited with having been the first to recognize the disease in man. However, Laennec was the earliest authority to describe and name them in the memoir which he read before the Society of the Faculty of Medicine of Paris in 1806.

Paget [2] was probably the first to call attention to the ability of moles to degenerate into malignant growths. Later, Virchow [3] recognized both a sarcomatous and a carcinomatous structure in many degenerated moles. He employed the term "melanoma" to describe the entire group.

Unna [4] presented his theory in favor of epithelial origin of nevus cells, and thus all melanomas arising from these cells were considered to be of epithelial origin. The promulgation of this theory stimulated considerable investigation in an attempt to determine the origin of these lesions, and various theories regarding their genesis were advanced; the majority of investigators were in favor of the theory that they were of epithelial origin. Unna's theory is supported, among others, by the

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Abridgment of this thesis submitted to the faculty of the Graduate School of the University of Minnesota in partial fulfilment of the requirements for the degree of Master of Science in Dermatology and Syphilology, 1931. Work done in the Section on Dermatology and Syphilology, the Mayo Clinic, while a Fellow in Dermatology and Syphilology, the Mayo Foundation.

1. Dupuytren, quoted by Pemberton, Oliver: Observations on the History, Pathology and Treatment of Cancerous Diseases, London, J. Churchill, 1858.

2. Paget, James: Lectures on Surgical Pathology, ed. 3, Philadelphia, Lindsay & Blakiston, 1865, pp. 639-645.

3. Virchow, R.: Pigment und diffuse Melanose der Arachnoides, Arch. f. path. Anat. u. Physiol. **16**:180, 1859.

4. Unna, P. G.: The Histopathology of the Diseases of the Skin, New York, The Macmillan Company, 1896, pp. 745-754.

following observers: Gilchrist,[5] Schalek,[6] Anthony,[7] Fox,[8] Dawson,[9] McCarthy,[10] Smith,[11] and Broders and MacCarty.[12]

Ribbert [13] gave the opinion that these lesions arise from mesoblastic chromatophores, and thus are sarcomas. Spencer [14] expressed the belief that the cells arise primarily in the epidermis, and that when the lesion is once started the mesoblastic cells take part in it, so much so that the structure of the secondary growth resembles sarcoma.

Ewing,[15] in his book "Neoplastic diseases," did not make a definite personal statement regarding the origin of these tumors, but later, in the *British Medical Journal*,[16] he stated:

> The work of Soldan and Masson has proved beyond reasonable doubt that the naevus cell is derived from and belongs to the peripheral sensory nerve end-organs. Whether this cell is neuro-ectodermal or mesoblastic is uncertain, but an epidermal origin seems to be excluded.

The choice of treatment for these lesions has aroused as much controversy as that of their genesis. There is considerable diversity of opinion regarding the advisability of removing the lesions by various surgical methods, of treating them by roentgen rays and radium or of leaving them entirely alone. It is interesting to read proceedings of

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5. Gilchrist, T. C.: Are Malignant Growths Arising from Pigmented Moles of a Carcinomatous or of a Sarcomatous Nature? Report of Two Cases (One in a Negro), with a Study of the Histogenesis of Pigmented Moles, J. Cutan. Dis. **17**:117 (March) 1899.

6. Schalek, Alfred: A Contribution to the Histogenesis of Melano-Sarcoma of the Skin, J. Cutan. Dis. **18**:145 (April) 1900.

7. Anthony, H. G.: The Developmental Defects of the Skin and Their Malignant Growths, J. A. M. A. **42**:1606 (June 18) 1904.

8. Fox, W. S.: Researches into the Origin and Structure of Moles, and Their Relation to Malignancy, Brit. J. Dermat. **18**:1 (Jan.) 1906.

9. Dawson, J. W.: The Melanomata: Their Morphology and Histogenesis, Edinburgh M. J. **32**:501 (Oct.) 1925.

10. McCarthy, Lee: Histopathology of Skin Diseases, St. Louis, C. V. Mosby Company, 1931, pp. 414-418.

11. Smith, D. T.: Evidence Showing the Existence of Two Distinct Types of Pigment Cells Capable of Giving Rise to Melanotic Tumors, Bull. Johns Hopkins Hosp. **36**:185 (March) 1925.

12. Broders, A. C., and MacCarty, W. C.: Melano-Epithelioma: A Report of Seventy Cases, Surg., Gynec. & Obst. **23**:28 (July) 1916.

13. Ribbert, Hugo: Ueber das Melanosarkom, Beitr. z. path. Anat. u. allg. Path. **21**:471, 1897.

14. Spencer, W. G.: Melanosis (Melanin: Melanoma: Melanotic Cancer), Brit. M. J. **2**:907 (Nov. 17) 1923.

15. Ewing, James: Neoplastic Diseases, ed. 3, Philadelphia, W. B. Saunders Company, 1928, pp. 919-931.

16. Ewing, James: The Problems of Melanoma, Brit. M. J. **2**:852 (Nov. 22) 1930.

various dermatologic meetings at which patients with melanomas were presented. Opinions vary greatly; some advised radical removal of the lesions, others advised that they be left alone.

Dupuytren laid down the principle that operation should not be performed when one is certain that one is dealing with a melanoma, whereas Dietrich [17] believed that early and wide excision was indicated.

Handley [18] expressed the opinion that the larger number of simple moles require no treatment whatever and should be left alone. He advised excision if the lesion was situated in an area subjected to irritation or if it showed signs of growth.

Bloodgood,[19] Keen,[20] and Coley and Houget [21] advocated prophylactic removal of all nevi about the body, lest they become malignant.

Broders and MacCarty reported the results of surgical treatment in seventy cases of melanoma studied at the Mayo Clinic. They stressed the necessity of early diagnosis, radical removal of the primary lesion and regional lymphatic nodes and prophylactic removal of nevi in areas subjected to irritation.

It is evident that the consensus favors early radical removal of lesions that appear suspicious. Many of the observers who have reported good results from noninterference with the lesions, and who have reported that their patients were alive and well for many years, must be considered as citing questionable cases of melanoma. The same is true when the lesions had been destroyed by various destructive agents, or by roentgen rays and radium, without first obtaining a specimen for biopsy. There is little doubt that a melanoma may be present for years without causing death, but one can never be sure that the lesion is a true melanoma except after microscopic examination.

Clinically, melanoma is often confused with benign pigmented nevus, pigmented basal cell epithelioma, verruca senilis, fibrosis with hemorrhage, hemangioma and "blue nevus" (described by Jadassohn and Tieche). Clinically, of course, all of these lesions present certain characteristics that allow one to make a fairly accurate diagnosis, but it cannot be conclusive without a microscopic examination of the lesion.

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17. Dietrich, quoted by Pemberton, Oliver: Observations on the History, Pathology, and Treatment of Cancerous Diseases, London, J. Churchill, 1858.

18. Handley, W. S.: The Pathology of Melanotic Growths in Relation to Their Operative Treatment, Lancet **1**:927 (April 6) 1907.

19. Bloodgood, J. C.: Moles, Pigmented and Nonpigmented, and Other Skin Defects in the Precancerous Stage, Northwest Med. **28**:543 (Dec.) 1929.

20. Keen, W. W.: The Danger of Allowing Warts and Moles to Remain Lest They Become Malignant: With Twenty-Five Illustrative Cases, J. A. M. A. **43**:96 (July 9) 1904.

21. Coley, W. B., and Hoguet, J. P.: Melanotic Cancer: With a Report of 91 Cases, Ann. Surg. **64**:206 (Aug.) 1916.

## CLINICAL AND MICROSCOPIC CHARACTERISTICS

An early melanoma is usually a slate-colored, or bluish-black nodule, varying in diameter from 0.5 cm. to several centimeters. The lesion may have a rounded or flat surface, and may be either raised or on a level with the surface of the skin. It is firm and bleeds easily. The color does not disappear on diascopic pressure. Occasionally one is able to see very fine, pigmented, radiating projections extending into the adjacent normal skin. This is usually a sign of early growth, and may shortly be followed by numerous pigmented satellite lesions, indicating local dissemination of the tumor. Later, the tumor may become ulcerative and fungoid in nature, and at this stage is usually accompanied by multiple metastatic cutaneous nodules.

Fig. 1.—Melanoma from the back of the hand. The origin of the malignant cells is definitely from the epidermis, and early invasion of the upper part of the cutis has taken place. Hematoxylin and eosin; × 100.

The cells of the majority of melanomas are undifferentiated and embryonal in appearance (fig. 1). Various types of cells are present; they may be round or cuboidal, spindle-formed or three-cornered, and may contain large, pale, elliptic nuclei or large, vesicular nuclei situated in any part of the body of the cell. The alveolar arrangement of these cells is characteristic; numerous mitotic figures are usually present. The basal cells are usually heavily laden with melanin, and melanoblasts and dendritic cells are present in the epidermis. Chromatophores, laden with melanin, are scattered throughout the cutis. At times one may see tumor cells invading the lymphatic structures and blood vessels.

Clinically, a blue nevus resembles a melanoma, but it is bluish gray or blue-black, round or oval, and slightly elevated. It is firm to

palpation and is most frequently situated on the face or extensor surfaces of the extremities. Histologically (fig. 2*A*), the epidermis and upper part of the cutis are usually normal. Circumscribed areas of extremely long and irregularly spindle-shaped cells containing melanin pigment are situated in the mid-cutis. They are usually benign, but occasionally undergo sarcomatous changes.

A pigmented basal cell epithelioma may be confused clinically with a melanoma. Histologically (fig. 2*B*), the lesion presents a typical picture of a basal cell epithelioma with melanin pigment in the basal cells of the epidermis and in the chromatophores of the cutis. Nevus cells are not present.

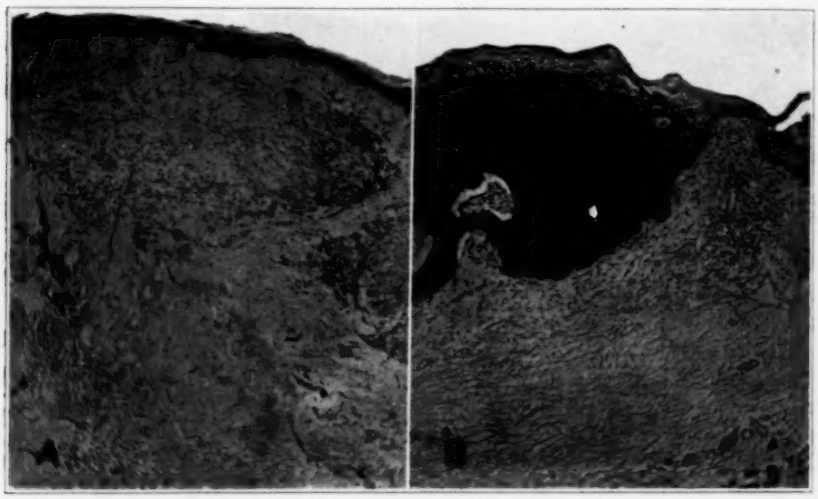

Fig. 2.—*A*, "nevus Blau." There are nests of pigmented cells in the middle part and upper third of the cutis. The epidermis is normal; × 42. *B*, pigmented, basal cell epithelioma. The origin of the basal cells from the epidermis and areas of melanin pigment in the epidermis are evident. Silver nitrate and hematoxylin; × 42.

Verruca senilis of the acanthotic solid type sometimes resembles melanoma. These lesions occur on any part of the body as sharply circumscribed, elevated, verrucous, brownish or black lesions, often appearing as though stuck on the skin and covered with a greasy scale. Histologically (fig. 3*A*), the picture is that of benign pigmented epithelial hyperplasia. No nevus cells are present.

As a result, possibly of slight trauma, many patients may present single or multiple subcutaneous bluish nodules indistinguishable clinically from melanomas. Histologically (fig. 3*B*), they present the picture of

fibrosis or angiofibroma with deposits of hemosiderin rather than melanin throughout the cutis.

The clinical picture of a pigmented nevus is well known, but in many cases microscopic examination is necessary to distinguish it from a melanoma. Histologically, if malignant change is taking place the cells will be embryonal in type and undifferentiated. Mitotic figures will be present, and the disorderly arrangement and varied types of cells will be evident.

The prognosis in cases of melanomas is more unfavorable than that of any other type of malignant neoplasm. Many investigators have maintained that treatment of any kind is of little value, and therefore believe that the lesions are better left entirely alone.

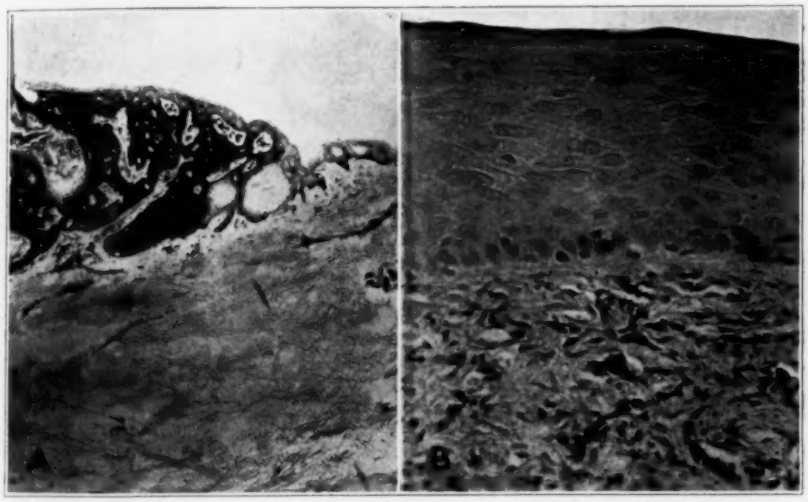

Fig. 3.—*A*, verruca senilis. There are hyperkeratosis, marked irregular acanthosis and melanin pigment in the epidermis. Silver nitrate and hematoxylin; × 35. *B*, fibrosis with hemorrhage. There are deposits of hemosiderin in the upper part of the cutis. Mallory's ferrocyanic stain; × 160.

In order to ascertain the value of this type of treatment, a large group of melanomas was analyzed. It was my intention to divide these cases into two groups: those in which treatment of various types had been given, and those in which there had been no treatment whatever, and to compare the average duration of life of the two groups of patients. However, in the 265 cases reviewed, there were only 6 patients who had no treatment of any kind. Obviously, this group is too small to allow deductions to be drawn. It was possible, however, to estimate the value of early and late operation, and the efficacy of roentgen rays and radium in the treatment of these neoplasms.

ANALYSIS OF CASES

*Age and Sex of Patients.*—The average age of the patients was 45 years; the youngest patient was 12 years of age, and the oldest, 81. There were 140 males and 125 females in this series. All literature reviewed revealed the incidence of melanotic involvement to be much higher among men than among women. This may be attributed to the fact that women are more solicitous about their appearance, and moles or nevi receive early attention.

*Incidence of Origin of Melanomas From Nevi.*—Most investigators are of the opinion that all melanomas arise from preexisting nevi. This has probably been exaggerated. There was a history of origin from nevi in only 50 per cent of the cases reported by Broders and MacCarty, and in 36.7 per cent of the cases reported by Horwitz.[22] In my series there was a history of origin from nevi in 60 per cent of the cases, and in 20 per cent of these the growths had been subjected to trauma. There were nine cases of melanoma following degeneration of birth marks.

*Appearance of New Lesions Following Excision of Primary Lesions (fig. 4A).*—One of the most disconcerting features encountered, following excision of primary melanomas, is the tendency for new lesions to appear at the site of excision. This occurred in 30 per cent of the cases in this series. The average interval between the time of excision and the appearance of new lesions in and around the scar was two years; the longest interval was fifteen years, and the shortest interval was three weeks.

Microscopic examination of a primary melanoma excised at the clinic disclosed tumor cells invading the lymphatic structures about 3 cm. beyond the border of the lesion. In most of these cases the excision was probably not wide or deep enough to include all of the tumor cells, or else local extension of the tumor cells to neighboring lymph or blood vessels had already occurred.

*Recurrences in Lymph Nodes.*—Recurrences occurred locally in the regional lymph nodes in 18 per cent of the cases in which the nodes were excised. The average interval between the time of excision and recurrence was two years; the longest interval was ten years, and the shortest interval was two months.

During the last few years roentgen rays have been used more and more in the treatment of extensively involved lymph nodes, and, as I shall show later, the results obtained are slightly better than those obtained by radical surgical procedures.

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22. Horwitz, Alec: Melanotic Tumors: Nonmelanotic Melano-Epitheliomas and Their Relation to the Melano-Epitheliomas, Ann. Surg. **87**:917 (June) 1928.

*Sites of Lesions.*—In reviewing the literature on the subject it was interesting to note the frequency with which melanomas were reported as occurring on the lower extremities. In the series reported by Horwitz, 57.1 per cent were on the lower extremities, and 34.7 per cent of them were on parts usually covered by shoes. In the series reported by Coley and Hoguet, 33 per cent were on the lower extremities in general and 18.7 per cent particularly were on the foot. Broders and MacCarty reported a series of seventy cases. The lower extremities in general were involved in 41.4 per cent of the cases, and the foot and ankle particularly in 22.8 per cent. In Dawson's series, 27 per cent occurred on the lower extremities, and of these, 19.4 per cent were on the foot.

In my series, the primary lesions were situated as follows: face, sixty cases; leg and thigh, forty-five; foot, forty-four; chest, thirteen; hand, ten; scalp, eight; back, twenty-eight; neck, twenty-seven; arm, fourteen; abdomen, thirteen, and penis, vulva and anus, each one case.

The face was involved in 22.7 per cent of the cases, the lower extremities in general in 33.6 per cent, and particularly the foot in 16.6 per cent.

It is probable that nevi are not situated on the face or lower extremities to any greater degree than on any other part of the body, but the lesions situated on these parts are subjected to greater trauma than those situated on other parts of the body.

*Delayed Metastasis.*—In spite of the high degree of malignancy, and the rapid onset of death following dissemination of metastatic growths, some persons seem to possess unusual resistance to invasion of the internal organs by these growths. It is probable that metastasis already has taken place at the time of excision of the primary growth, but many years may elapse before death occurs from metastasis. There were nine cases of delayed metastasis in this series. The interval between the time of excision of the primary growth and demonstrable evidence of metastasis varied from five to twelve years. Many theories have been advanced to explain this phenomenon, and the subject has been recently reviewed by Wilbur and Hartman.[23] This phenomenon of delayed metastasis further illustrates the necessity of giving a very guarded prognosis in all cases when one is dealing with a melanoma.

*Internal Organs Involved by Metastasis.*—The liver was the internal organ most commonly invaded by metastatic growth; invasion of the lungs was second in frequency, and the brain, third. In most cases, of course, there was metastasis to all of the internal organs, but before death the patient most frequently presented symptoms referable to the aforementioned organs. One patient examined at the clinic, and treated

23. Wilbur, D. L., and Hartman, H. R.: Malignant Melanomas with Delayed Metastatic Growths, Ann. Int. Med. **5**:201 (Aug.) 1931.

for Addison's disease, at necropsy gave evidence of marked melanotic malignancy of the suprarenal glands.

*Melanotic Whitlows (Fig. 4B).*—In 1886, Hutchinson [24] named and described the condition known as "melanotic whitlow." It closely resembles the ordinary inflammatory whitlow. In the melanotic type of whitlow, however, the region of inflammation is surrounded by a very fine black border, looking as if the part had been touched with silver nitrate. If the disease is unrecognized, and treatment is the same as that for ordinary whitlow, a fungating lesion soon develops, with loss of the nail and involvement of the regional lymph nodes. In general, metastasis is much slower in cases of this type and early recognition and amputation of the affected phalanges offers a fair hope of recovery.

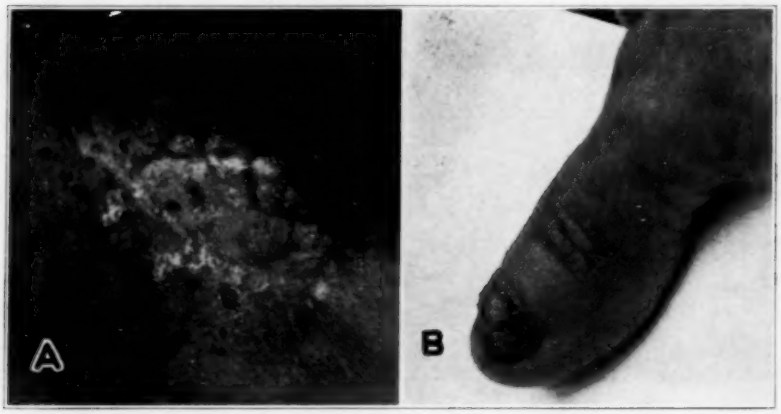


Fig. 4.—*A*, spray-like recurrence of melanoma in a scar, after the fourth excision in four years. *B*, melanotic whitlow. The normal thumb was injured with a hammer. Six months later, there was metastasis to the axilla. The finger was amputated, and treatment by roentgen rays was applied to the axilla. Death occurred nine months later.

Womack [25] reported a series of subungual melanomas, together with pathologic studies, and concluded that 15 per cent of all melanomas at the Barnes Hospital in St. Louis were of the subungual type. He advised early amputation of the involved phalanx with dissection of the regional glands.

There were six cases of melanotic whitlow in my group of cases. There were only three replies to follow-up letters. One patient died nine months after amputation of the thumb and radical dissection of

24. Hutchinson, Jonathan: Melanosis Often not Black: Melanotic Whitlow, Brit. M. J. **1**:491 (March 13) 1886.

25. Womack, N. A.: Subungual Melanoma: Hutchinson's Melanotic Whitlow, Arch. Surg. **15**:657 (Nov.) 1927.

the axillary glands. Two patients who gave no evidence of metastasis at the time of examination, lived for three and a half and four and a half years, respectively, following amputation of the involved phalanges.

*Implantation Melanomas (Fig. 5A).*—Eve [26] reported a series of cases to which he gave the name "implantation melanomas," because of the fact that months or years after occurrence of a puncture wound of the palm or sole, melanoma developed at the site of injury. He believed that melanomas were produced by traumatic implantation into the subcutaneous tissue of dendritic cells which are normally found in the epidermis.

There were two cases of this type in my series. Both patients gave histories of having had puncture wounds produced by tacks in their shoes. One patient died two and a half years after the initial injury.

Fig. 5.—*A,* "implantation melanoma." This lesion followed an injury from a tack in a shoe. *B,* melanoma of eight years' duration originating from a nevus on the right forearm. It was widely excised Dec. 18, 1930, at which time there was no metastasis.

In the second case, ulceration occurred one year after injury. When examined at the clinic, the patient presented a fungating lesion, 2 by 3 cm. in diameter, and having a faint, black, pigmented area at the border of the ulcer. There were several metastatic nodes in the groin, and a roentgenogram of the thorax gave evidence of extensive metastatic involvement of both lungs. The patient died three and a half years after injury.

Early recognition of this type of lesion is as difficult and as important as recognition of the whitlow type of lesion. A history of a puncture wound, followed by an ulceration that is refractory to ordinary

26. Eve, Frederic: A Lecture on Melanoma, Practitioner **70**:165 (Feb.) 1903.

measures of treatment, should be looked on with suspicion, and a careful search should be made for the pigmented area at the border of the ulcer. If necessary, biopsy should be obtained.

Early amputation of the foot probably offers the only hope for recovery.

*Analysis from the Standpoint of Length of Life.*—Of the 265 patients examined at the clinic, I was able to trace only 188 whose cases were suitable for analysis from this standpoint. It was necessary to divide them into five distinct groups.

Group 1 was composed of those patients who had undergone surgical treatment elsewhere, who when examined at the clinic were suffering from varying degrees of metastasis, and on whom subsequent operations were not performed. As nearly as could be determined from the histories obtained from these patients, there was no metastasis at the time of the initial operation. General data are given in the table. Of the eleven patients who have remained alive and well for five years or more, one each has lived eighteen, twelve, ten, nine and eight years; two each have lived seven, six and five years.

Group 2 was composed of patients who had undergone surgical treatment elsewhere, who when examined at the clinic gave evidence of varying degree of metastasis, and on whom further surgical intervention was considered necessary (table). Of the four patients who have remained alive and well for five years or longer, one each lived fourteen, ten, nine and eight years.

Group 3 was composed of patients examined at the clinic who had had no previous surgical treatment (table). Of those who gave evidence of metastasis at the time of operation at the clinic, only one patient was alive and well at the end of five years. Of those who gave no evidence of metastasis at the time of operation at the clinic, eleven remained alive and well for five years or more. One each lived twelve and a half, twelve years, nine and six years; four lived five and a half and three lived five years.

Group 4 was composed of patients treated with roentgen rays or radium (table). Only two patients were alive five years after beginning treatment. All of these patients had such extensive metastasis at the time of examination that they were considered inoperable, and radiation was given only as a palliative measure. Only two patients were examined at the clinic who had had roentgen rays as the only treatment for the primary lesion. These treatments were given elsewhere, and when the patients were examined at the clinic, metastasis was so extensive that roentgen therapy was continued. One of these patients lived for two years; the other died after five and a half years.

Group 5 was composed of patients who had nonmelanotic melano-epitheliomas (table).

Nonmelanotic and melano-epitheliomas frequently arise from non-pigmented nevi that have been traumatized. In many cases, however, the primary lesion may be pigmented, and the metastatic growths may appear as nonpigmented tumors; the reverse is also true. Clinically, they run the same course, but the condition in the nonpigmented group is thought to be slightly more malignant than that in the pigmented group.

Broders and MacCarty maintained that nonmelanotic melanomas belong to the same class as the true melanomas, and differ only in their lack of pigment. They have the same cellular appearance as the non-

*Length of Life of One Hundred and Eighty-Two Patients with Melanoma* *

| Group | Cases | Dead | | Span of Life | | |
|---|---|---|---|---|---|---|
| | | Patients | Per Cent | Average, Months | Longest, Years | Shortest, Months |
| Primary operation elsewhere, metastasis when examined at clinic, and no operation at clinic | 42 | 31 | 75.8 | 46† | 20 | 3 |
| Primary operation elsewhere, metastasis when examined at clinic, and operation at clinic | 27 | 23 | 85 | 20‡ | 14 | 2 |
| Primary operation at clinic | | | | | | |
| Metastasis at time of operation | 22 | 21 | 95.4 | 21‡ | 12½ | 18 |
| No metastasis at time of operation | 26 | 15 | 57.7 | 54‡ | | |
| Treatment by roentgen rays or radium | 45 | 43 | 95.5 | 30§ | 5 | 1¼ |
| Nonmelanotic melano-epitheliomas | 20 | 17 | 85 | 16§ | | |

* In six other cases diagnosis was uncertain. These are not included in the table but are analyzed in the text.
† From time of operation done elsewhere than at the clinic.
‡ From time of operation done at the clinic.
§ From time of first treatment at the clinic.

pigmented regions in melanomas, and Broders and MacCarty have expressed the belief that if the cells of the nonmelanotic tumors were given the opportunity to differentiate enough, they would produce melanin pigment. Formation of pigment is a kind of "differentiation," and cells that are forming pigment are slightly less malignant than those which are not.

Histologically (fig. 6), the cells that go to make up a nonmelanotic melano-epithelioma are greatly diverse in shape. At times the picture may be that of a fibrosarcoma, the cells being markedly elongated and arranged in bundles. At other times an alveolar arrangement of the cells is predominant, and in some cases the malignant cells are so arranged as closely to resemble a large round cell or small round cell sarcoma. The forms of individual cells very. They may be spindle-shaped, round, oval or elongated. Numerous mitotic figures are usually present. Horwitz has expressed the opinion that this variation in form is evidence of different stages of "differentiation" or regression

to a more embryonal state of development. This, with the absence of pigment, explains the highly malignant nature of nonmelanotic melano-epitheliomas.

All of the patients represented in the table had varying degrees of metastasis when examined, and they were treated by roentgen rays, or operation, or both. Only one patient was alive and well five years later.

Six patients were examined at the clinic who presented lesions that were diagnosed clinically as melanomas. None of them had had treatment of any kind before coming to the clinic. They were advised to have the lesions removed but refused. Follow-up letters sent to these patients elicited replies that all were alive and well for from five to ten

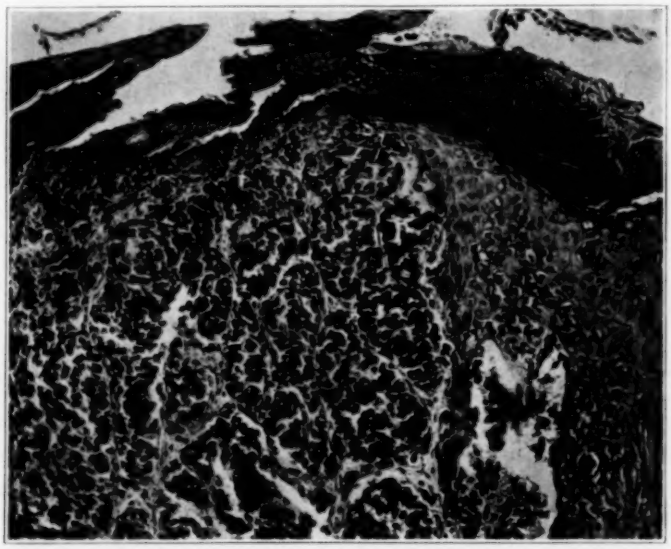

Fig. 6.—Nonmelanotic melano-epithelioma. The section was taken from a nodule on the right arm. The origin from the epidermis and the alveolar arrangement of the malignant cells are evident. Pigment is absent. Hematoxylin and eosin; × 100.

and a half years after their examination. All reported that there was no increase in growth of the lesions, nor was there any evidence of "lumps" anywhere on the body.

## COMMENT

There was marked difference in the span of life of patients who received early surgical treatment on the one hand, and of those who had received surgical treatment after metastasis had occurred.

In the former group there were sixty-eight patients (59.1 per cent) who lived an average of four years and ten months; in the latter group

were sixty-nine patients (88.1 per cent) who lived an average of two years and seven months.

The results obtained by the use of roentgen rays or radium in the treatment of late cases at the Mayo Clinic are practically the same as those obtained by radical surgical procedures. Of patients who have received either type of treatment, 95.5 per cent are dead; the span of life of those treated surgically is one year and nine months, and of those treated with roentgen ray or radium, two and a half years.

Although melanomas are notoriously resistant to roentgen rays, the outlook in late cases of melanoma is very poor in any event, and rather than subject the patient to radical surgical procedures it would probably be better to give intensive roentgenologic treatment as a palliative measure. If metastasis is discovered early, and only a few discrete lymph nodes are involved, excision is the method of choice, followed by massive doses of roentgen rays to the involved region.

It was impossible to determine the value of roentgen rays in treatment of initial lesions because of the small number of cases of that type examined at the clinic. Neither roentgen rays nor radium was used in the treatment of primary lesions at the clinic. In using these therapeutic agents on primary lesions, one can never be sure, without resorting to biopsy, whether one is dealing with a true melanoma or a benign pigmented lesion, and the question can probably never be settled if metastasis does not occur.

The nonpigmented type of melanoma is generally thought to be more malignant than the pigmented type. In this series of cases, however, there was very little difference in prognosis. Among those patients who had either type of lesion, and metastasis had taken place, 85 per cent are dead. However, patients with the pigmented type of growth have, on the average, lived one year longer than those with nonpigmented tumors.

In the six cases in which the diagnosis was questionable it could not be proved without biopsy or prolonged observation. In at least two of these cases, the growth probably was melanoma. The fact that none of the six patients has died does not prove that the lesions were not true melanomas. Such cases always raise the question whether many of these lesions are better if left entirely alone. Since the mortality rate following surgical treatment is so high, it seems that certain lesions situated so as not to be subject to trauma should not be interfered with unless they show signs of growth. It is well known that such lesions may remain for years without signs of growth, but immediately following excision or other types of treatment, metastasis occurs and death soon follows. It is possible that malignant cells lie dormant in the tissues adjacent to the lesion and are "stirred up" by attempts at removal of the growth.

## SUMMARY AND CONCLUSIONS

The histories of 265 patients with melanomas who were examined at the Mayo Clinic are analyzed. Various types of melanomas are described. Clinical and histologic descriptions are presented, and the differential diagnosis of allied lesions is considered.

Of these 265 cases, 188 were suitable for analysis from the standpoint of prognosis. The data resulting from this analysis are summarized in the table.

The dangerous type of mole is slightly elevated, with a thin, smooth covering of epidermis, steel blue or blue black, and situated in an area subjected to trauma. Lesions of this type should be radically excised early. About 4 cm. of normal skin on all sides of the lesion should be included, and the incision should be deep enough to include the subcutaneous tissue.

When the regional lymph nodes are extensively involved by metastasis, intensive roentgenologic treatment should be instituted in preference to radical surgical treatment. However, when only a few discrete metastatic nodes are present it is probably better to excise them and follow up with heavy doses of roentgen rays or radium.

Early, radical removal of any type of nevus subjected to trauma is the only means of reducing the high mortality rate of melanomas.

# PHENOLPHTHALEIN ERUPTION

## EXPERIMENTAL DATA ON ITS CAUSATION

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In 1918, Abramowitz [1] proved definitely that some chronic, recurring, fixed pigmentary eruptions could be caused by an idiosyncrasy to phenolphthalein. Since that time, many cases have been reported in which the same etiologic agent has been found. Phenolphthalein is also known to produce urticaria [2] and herpes simplex [3] besides the classic picture of a fixed pigmentary dermatitis. Similar eruptions are produced by antipyrine, arsphenamine and amidopyrine.

Considerable discussion has arisen as to how this dermatitis is produced. Wise and Abramowitz [4] felt that it was most likely due to some split product of phenolphthalein in the body. Pollitzer [5] has held similar views and suggested that the phenol radical might be the exciting agent. The general consensus is that it is due to impurities in the drug, because toxic effects have been alleged to be more frequent with the use of so-called yellow phenolphthalein, which contains large amounts of resinous by-products, than with the so-called white phenolphthalein, which is relatively pure.

Phenolphthalein is produced by combining phenol with phthalic anhydride, which gives phenolphthalein and some organic by-products. These by-products seem to be high in anthraquinone derivatives and are extremely difficult to remove entirely by the usual processes of purification. Abel and Rowntree [6] administered large doses of phenolphthalein

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Studies and Contributions of the Department of Dermatology and Syphilology of the University of Michigan Medical School, Service of Dr. Udo J. Wile.

1. Abramowitz, E. W.: Erythema Multiforme Associated with Cutaneous Pigmentation (Melanin): Clinical and Pathological Report of Five Cases, J. Cutan. Dis. **36**:11 (Jan.) 1918.

2. Corson, E. F., and Sidlick, D. M.: Urticaria from the Habitual Use of Phenolphthalein, J. A. M. A. **78**:882 (March 25) 1922.

3. Rosenbloom, J.: Report of a Case of Nasal Herpes Due to Ingestion of Phenolphthalein, J. A. M. A. **78**:967 (April 1) 1922.

4. Wise, F., and Abramowitz, E. W.: Phenolphthalein Eruptions, Arch. Dermat. & Syph. **5**:297 (March) 1922.

5. Pollitzer, S., in discussion of Wise and Abramowitz (footnote 4).

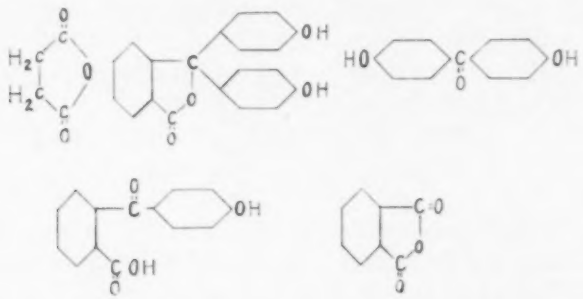
6. Abel, J. J., and Rowntree, L. G.: Action of Some Phthaleins and Their Derivatives, J. Pharmacol. & Exper. Therap. **1**:232, 1909.

without a toxic effect. The drug as such has been recovered from the excretions of the body up to about 90 per cent. A mild transient albuminuria has been reported in a few cases by Hydrich.[7]

I have been unable to find experiments carried on with the idea of determining whether any of the split products of phenolphthalein would reproduce the eruption in a susceptible person.

With regard to experiments on local sensitization, Abramowitz [1] in his first cases attempted to produce local lesions with the scratch method and subcutaneous injections, without results. Sulzburger [8] has obtained negative patch tests.

The present knowledge of the causation of phenolphthalein dermatitis is still open to question. During the past year I have had a striking case in which the eruption has been due to phenolphthalein, and during the patient's stay in the hospital it was possible to carry on a



series of experiments bearing on the question of the toxic nature of the split products and impure varieties of the drug. An additional line of investigation was made possible in testing out a chemically pure phenolphthalein made by a new method. Prof. F. Blicke and Dr. Weinkauff of the College of Pharmacy allowed me the use of this phenolphthalein and other organic compounds.

## REPORT OF A CASE

*History.*—Miss E. R., aged 20, entered the University Hospital on Sept. 5, 1930, complaining of an itching generalized eruption. Two and a half years previously she had noticed an eruption involving the arms and legs and the region about the mouth. The lesions were about the size of a pea and intensely pruritic. They lasted from three to four days and then faded, leaving some pigmentation. Similar attacks

7. Hydrich, J. L.: Albuminuria Following the Ingestion of Phenolphthalein, Proc. Am. Soc. Biol. Chem., 1914, p. 36, quoted by Wise and Abramowitz (footnote 4).

8. Sulzburger, M. B., in discussion of Ayres, S., and Anderson, N. P.: Dermatitis Medicamentosa Due to Ephedrine; and James, B.: Procaine Dermatitis, J. A. M. A. **97**:442 (Aug. 15) 1931.

had occurred every three to six months since, then with a recurrence in the old areas and also the appearance of new lesions. The present exacerbation was much more severe than any of the preceding ones. For a number of years the patient had been slightly constipated and for the past three to four years she had been taking "Feenamint" for relief from this condition.

The patient had always been in good health, and nothing in the past history was of significance. There was no history of any unusual idiosyncrasies.

The family history likewise did not reveal any tendency toward sensitization or abnormal reaction to drugs.

*Examination.*—The patient was a well nourished and well developed young woman of 20. She presented a generalized eruption which was most marked over the trunk and arms. There were a few lesions about the mouth and genitalia. The mucosa were clean. The eruption was made up of irregular and somewhat indefinite macules varying in size from that of a dime to that of half of a palm. They all presented a striking color. For the most part they were deep purple in the center with an irregular lighter reddish purple at the periphery. The lesions about the lips and sacrum had a slight scale. On pressure there was no tendency for the pigmentation to fade. There was no infiltration or edema associated with any of the lesions at this time. A clinical diagnosis of dermatitis medicamentosa due to phenolphthalein was made.

Laboratory examinations showed no abnormal observations. The Kahn test was negative. Examination of the urine for albumin and sugar gave repeatedly negative results. A test for phenolphthalein in the urine was not performed. Examination of the blood showed: hemoglobin, 105 per cent, red cells, 4,910,000 and white cells, 8,500. The differential smear was normal, except for a slight increase in eosinophils (3 per cent).

The patient was advised against the use of phenolphthalein or any proprietary preparations that might contain it. She was seen several times in the ensuing months, and the eruption appeared to be fading gradually.

*Course.*—On May 21, 1931, approximately nine months from the time she was first seen, she appeared in the clinic with an acute and extensive exacerbation. No definite history of ingestion of phenolphthalein could be obtained. She had, however, been using mineral oil for constipation. Whether or not she had recently used a preparation of mineral oil containing phenolphthalein could not be determined. All of the old lesions were more deeply pigmented, and the borders had a more erythematous appearance. The smaller patches had taken on an urticarial aspect, showing only a slight amount of purple in the center and a broad halo of erythema. These patches also had an associated localized edema and were extremely pruritic.

It was decided to hospitalize the patient for further observation, and, under an eliminative regimen of forced fluids and large daily doses of magnesium sulphate, the acute part of the eruption rapidly subsided in three days, leaving only the pigmented areas.

## EXPERIMENTAL DATA

*Effect of an Ordinary Preparation of Phenolphthalein.*—After the eruption had involuted so that only the pigmented macules remained, the patient was given a "patent medicine" phenolphthalein tablet containing 1 grain (0.065 Gm.) of phenolphthalein, aromatics and enough sugar to make 5 grains (0.324 Gm.), in order to substantiate the clinical diagnosis. In about one hour the patient complained of being very uncomfortable and of a great deal of itching and burning. The

erythematous element in the lesions reappeared with marked edema. They all appeared much larger. The pigmentation was deeper. This reaction subsided in a few days.

*Effect of Other Drugs Producing Fixed Eruptions.*—Antipyrine, amidopyrine and neoarsphenamine are three drugs which in susceptible persons will produce an eruption simulating that due to phenolphthalein. It was thought that it would be of interest to see whether this patient who definitely had an idiosyncrasy for phenolphthalein would also have an idiosyncrasy for other drugs producing a similar eruption. She was given 5 grains of antipyrine by mouth, and there was no reaction in forty-eight hours. No result was obtained with 5 grains of amidopyrine. Then she was given 0.3 Gm. of neoarsphenamine intravenously; this likewise produced no demonstrable effect in forty-eight hours. Therefore, one can conclude that an idiosyncrasy for one drug producing a fixed eruption does not necessarily indicate susceptibility to the whole group.

*Effect of Some of the Split Products of Phenolphthalein.*—Phenol: The patient was given 1 drop of pure phenol in milk, which is an amount far in excess of the amount of phenol which may be "split off" from 1 grain (0.065 Gm.) of phenolphthalein. No reaction was noted at any time.

Phthalic Anhydride: The patient was given 0.5 Gm. of phthalic anhydride, and two hours later she felt as though she were going to have an exacerbation. There were a few small urticarial wheals. The old pigmented lesions showed no change. This eruption cleared up promptly. She was then given 1 grain of phthalic anhydride and no reaction occurred, and we felt that the transient urticaria was probably produced on another basis as the original eruption showed no exacerbation.

p,p'-Dihydroxybenzophenone: p,p'-dihydroxybenzophenone is an organic compound similar in structure to phenolphthalein, except that benzoic acid nucleus has been split off. One-half grain (0.0324 Gm.) of this preparation produced no effect on the eruption.

p-Hydroxy-o-benzoylbenzoic Acid: p-hydroxy-o-benzoylbenzoic acid is a compound formed by the splitting off of one of the phenol radicals from phenolphthalein. The patient was given 0.5 grain (0.0324 Gm.) of this substance by mouth with no reaction.

Succinic Anhydride: Because of the similarity of structure between succinic anhydride and phthalic anhydride, it was thought of interest to administer the former substance. This was given the patient in a one-half grain dose with no noticeable effect.

From the aforementioned observations in which some of the split products of phenolphthalein have been used, it is evident that none produced an exacerbation of the eruption. There was a slight urticaria at the time of the administration of one-half grain of phthalic anhydride. Because of the fact that none of the pigmented lesions flared up, and because the eruption was so mild and transient, it was felt that this was a coincidental rather than a positive finding. Also the larger dose of phthalic anhydride administered later produced no effect.

*Effect of a Chemically Pure Phenolphthalein.*—Dr. Blicke and Dr. Weinkauff prepared this chemically pure phenolphthalein by a new synthesis[9] by means of which neither anthraquinones or resinous substances are produced as by-products.

The patient was given 1 grain of this chemically pure phenolphthalein, and within two hours she had a violent reaction (photographs). She complained of

9. Blicke and Weinkauff: J. Am. Chem. Soc. **54**:1446 (April) 1932.

itching and some pain and pressure over the lesions. The patches themselves had a brilliant areola about them. They were darker in the center and many had an infiltrated feel. This reaction simulated in all ways that produced by commercial phenolphthalein, except that it was more severe.

*Patch Tests.*—Patch tests were carried out to determine whether any local reaction could be obtained. Each substance tested was put on the skin in two

Photographs of the patient, showing (*A*) the fixed eruption in a quiescent stage, and (*B*) the eruption twelve hours after the ingestion of 1 grain of chemically pure phenolphthalein.

places, on the normal skin and on a patch of pigmentation. Phenolphthalein, phthalic anhydride, dihydroxybenzophenone and p-hydroxy-o-benzoylbenzoic acid were used. All gave entirely negative results at the end of forty-eight hours.

## SUMMARY

A case is reported in which the eruption was clinically that due to an idiosyncrasy for phenolphthalein. An exacerbation of the eruption

followed the ingestion of 1 grain of commercial phenolphthalein, thus substantiating the clinical diagnosis.

Other drugs producing fixed eruptions, namely antipyrine, amidopyrine and neoarsphenamine, produced no effect in this case. From this fact one would surmise that the causes of fixed eruptions are not from a common source but probably result from many different drugs.

Various split products of phenolphthalein were then given the patient in an effort to determine if possible whether any of them could be the exciting agent for the eruption.

Chemically pure phenolphthalein free from all by-products ordinarily found in commercial phenolphthalein was used to determine definitely whether the reaction to phenolphthalein was produced by impurities in the commercially used drug, or whether the reaction was one of the whole molecule.

Patch tests for local reaction were performed with phenolphthalein and some of the split products.

## CONCLUSIONS

1. The recurring pigmented eruption associated with the ingestion of phenolphthalein is due to phenolphthalein as a molecule and not to any of its known split products.

2. Sensitization to phenolphthalein in a patient does not necessarily carry with it an idiosyncrasy to other similar drugs in producing a fixed eruption.

3. Phenol, phthalic anhydride, dihydroxybenzophenone, p-hydroxy-o-benzoylbenzoic acid, which are the split products of phenolphthalein, did not produce the eruptive phenomena when ingested separately.

4. Patch tests with phenolphthalein and its derivatives gave negative results.

5. Chemically pure phenolphthalein produced a rapid and severe exacerbation, suggesting that the eruption is due to the phenolphthalein itself and not to any impurity or split product.

It is therefore contended that the fixed eruption of phenolphthalein is due to a reaction in the individual to the fixed molecule and not to any of its split products.

Dr. U. J. Wile allowed me to present this material.

# GRANULOMA PYOGENICUM

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In the field of medicine, granuloma pyogenicum has quite a recent history. In 1897, Poncet and Dor first brought the matter to the attention of the surgeons in France under the name of botryomycoma, a name that still clings to it in that country. However, the name, granuloma pyogenicum, proposed by Hartzell, is to be preferred. That this condition so long escaped clinical notice is strange, as it frequently causes great anxiety to the patient, and both in its appearance and in its liability to recur after removal bears sufficient symptoms to leave a lasting impression as a clinical entity.

In its simplest form granuloma pyogenicum appears as a small bright red ball of granulation tissue attached to the skin or mucous membrane by a pedicle, and it is frequently attributed to a slight wound. Anatomically, it consists of a mass of granulation tissue more or less organized into fibrous tissue. It is so vascular, that in some instances the richness in blood vessels makes it decidedly collapsible.

As previously mentioned, a pedicle, sometimes a very delicate one, may be present, and the patient or his friends may be seized with the desire to tie a string around it and thus strangle it. Even physicians unacquainted with the nature of this lesion may do this or may clip it off, leaving a stump. Such an inadequate removal is followed by a prompt recurrence, and, as Frieboes has remarked, the recurrent tumor strange to say usually halts in its growth at its original size, whether it be that of a pea, a cherry or a nut. Another peculiarity is that no matter how much these lesions may be irritated they do not grow any larger than the limit of volume in that individual case.[1] Not long ago we saw one that had existed for several years on the inner surface of the lower lip, and though subject to frequent injuries by the teeth and frequent bleedings, it had maintained an invariable size.

In our series there were in all fifty-five cases, thirty-nine of which were in women and sixteen in men. We do not know how to account

1. Frieboes, Walter: In den verschiedenen Grössenstadien macht das Wachstum spontan Halt, und dann bleiben meistens diese Tumoren trotz aller Reitzungen auf der gleichen Grösze stehen, Lehrbuch der Hautkrankheiten und Geschlechtskrankheiten, Leipzig, F. C. W. Vogel, 1930, p. 398.

for the greater preponderance of cases in women, as surely men are more subject to wounds and to infection than women, and, as previously mentioned, wounds, slight it is true, are often given as a cause of these tumors. As a strange contrast, Legroux (Thèse de Paris, 1904) found granuloma pyogenicum more frequent in men than in women, and in a percentage almost the opposite of ours.[2] In his series there were thirty-two cases in men and eighteen in women. In his series, therefore, 64 per cent of the cases were in males and 36 per cent were in females, and in ours, 29 per cent were in males and 71 per cent were in females. The difference was probably due to the type of patient, and shows how fallacious statistics may be.

The incidence of age is also interesting. The average age in forty-four cases was 45, and thirty of the forty-four patients were 45 years or over, so that the disease is one of middle and later life. Two of our cases occurred in children, one patient was a girl of 15. If small wounds were a dominant cause, surely children would be affected more frequently. It looks as if susceptibility, or rather tissue reaction, were more important than either traumatism or the infective agent. As regards occupation, that of housewife comes up with monotonous regularity, for the reason that most women of 45 or beyond are either housewives or retired to a hotel. The only cases in which the histories show that the patients were particularly exposed to wounds and infection were those of a ranch hand, a waitress and a woman physician. It has been said that the disease occurs more frequently in the uncleanly, but we have not found it so.

In five cases four of which were in women and one in a man, the lesion was situated in a nail-fold of a finger. We received the impression that it was possible that a tumor in this situation sometimes arose from an infected wart. Manicuring may also be a contributing cause, but this is an inference, not a direct observation.

In regard to the frequency of this condition there are few data obtainable. For a short time, about ten years, after Poncet and Dor's communication in 1897, the number of cases reported increased, both in France and in Germany; after this they decreased, owing, Skitzer thinks, not to an actual decrease but rather to a slackening in interest. In the Pathological Institute in Freiburg in ten years (1910-1920) Luchs saw twenty-six cases; in the Skin Disease Clinic in Breslau (1920-1927) there were seven cases. A few other cases have been reported in various countries all over the world.[3] Since interest has been shown in the condition, a number of cases have been reported in North America.

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2. Lenormant, C.: La prétendue botryomycose humaine, Ann. de dermat. et syph. **1**:161, 1910.

3. Spitzer, R.: Geographische Verteilung der Hautkrankheiten, in Jadassohn, J.: Handbuch der Hautkrankheiten und Geschlechtskrankheiten, Berlin, Julius Springer, 1928, p. 284.

One of the main reasons why these cases do not receive the individual attention they should is that they are referred to surgeons who regard them as instances of exuberant granulations, or, as the laity would say, "proud flesh," which undoubtedly they are, but they are exuberant granulations of a peculiar kind, and act in a peculiar way, and are therefore worthy of a special name and of special clinical attention.

The personal histories in a number of these cases show better than can general terms the peculiarities of the course, the difficulties of diagnosis and the application of the means of treatment.

*Locations of Granulomas Reported in This Paper* *

| | | |
|---|---|---|
| Hand | | 13 |
| Thumb (side of) | 1 | |
| Pulp of finger | 2 | |
| Finger (side of) | 2 | |
| Nail-groove of finger | 4 | |
| Nail-groove of thumb | 1 | |
| Back of hand | 3 | |
| Lower lip (red of) (2 lesions on one lip) | | 7 |
| Upper lip (red of) | | 1 |
| Mouth | | 10 |
| Corner of mouth | 1 | |
| Cheek pouch | 2 | |
| Lower lip (internal surface) | 2 | |
| Hard palate | 2 | |
| Gum | 3 | |
| Scalp | | 2 |
| Face | | 9 |
| Cheek | 5 | |
| Nose | 3 | |
| Upper lip (cutaneous surface) | 1 | |
| Earshell | | 2 |
| Back | | 1 |
| Umbilicus | | 1 |
| Calf of leg | | 1 |
| Foot | | 1 |
| Sole | | 2 |

* Situations of six were not stated in notes.

## REPORT OF CASES

*Granuloma Pyogenicum of the Hand.*—In thirteen of our fifty-five cases the tumor appeared on the hand, and of these ten were on the digits and three on the back of the hand.

CASE 1.—One of these tumors was a lobulated growth on the ulnar side of the left thumb, as large as the end of the thumb and of three months' duration. At first it was a small red dot under the skin, which the patient, a woman 27 years of age, pricked with a needle; it bled freely, and afterward became exuberant, with frequent free bleeding. Two large nodules were removed with the scissors without exciting pain. The removal of a third nodule, which was closely attached to the skin, was accompanied by pain, and a freely bleeding artery was exposed, which necessitated ligation. The tissue removed was soft and spongy.

CASE 2.—A lawyer, 53 years of age, had a pea-sized pedunculated granuloma pyogenicum on the radial side of the terminal phalanx of the left middle finger

which bled profusely on the slightest occasion. He said that at first it was a dark spot which he pricked with a pin or a knife point, causing profuse bleeding.

This history of an antecedent dark spot recurs in the histories of patients, and makes one reflect as to whether the traumatism was really the initial lesion or whether the growth preceded the traumatism.

We curetted the lesion thoroughly and applied trichloracetic acid, and secured permanent healing.

Case 3.—A woman, 52 years of age, said that a pinhead-sized white spot appeared on the pulp of the left index finger six weeks before she consulted us. This developed into a red spot, slightly elevated, which bled easily. The tension caused by the dilating blood vessels under the thick epithelium of the volar surface might easily cause the lesion to be white at first. This case is remarkable as being the only one with a precedent white spot that we have had. Lenormant reported a similar case in a woman 26 years of age with a large pea-sized tumor situated near the external border of the palmar surface of the right index finger. About a month previously the patient had noticed a white papule or elevation in this situation, which she opened with a pin. A few days afterward a reddish nodule appeared, which steadily grew.[2] We first curetted the lesion and cauterized the base with trichloracetic acid, and then administered thorough irradiation with radium, as from the history we surmised that the deep-lying vessels were affected.

Appearance of granuloma pyogenicum. It consists of a mass of granulation tissue more or less organized into fibrous tissue.

Nevertheless, the lesion still continued to have a raised curb about it, and the following month we cauterized it again, this time with a more penetrating caustic, the acid nitrate of mercury, after which normal healing was obtained.

Case 4.—A woman, 72 years of age, had a pedunculated granuloma pyogenicum half the size of a large walnut on the back of the left hand. The tumor was excised, and the base well irradiated with radium. Healing was uneventful. Three years afterward, the patient became affected with sarcomatosis, with spontaneous fracture of the left femur. No connection, however, could be established between the granuloma and the subsequent sarcoma.

*Granuloma Pyogenicum of the Red of the Lips.*—Granuloma pyogenicum assumes a special interest when situated on the red part of the lip, especially the lower lip, because of the liability of being mistaken for epithelioma.

Case 5.—A woman, 65 years of age, consulted us on account of a granuloma pyogenicum of the red part of the lower lip that had first appeared three years previously after convalescence from pneumonia. It was treated by the late Dr. Painter with the roentgen ray and disappeared. However, it recurred after a considerable time and was treated by us by curettement and trichloracetic acid. Two years subsequently, it again recurred. We saw the patient for two years more, during which time there was no recurrence.

CASE 6.—A girl, 18 years of age, said that her lower lip had been bitten two months previously, and a tumor subsequently appeared, a granuloma the size of a large pea. It first received an irradiation with radium and then was curetted and cauterized with trichloracetic acid, after which it healed uneventfully.

CASE 7.—A man, 60 years of age, consulted us on account of a granuloma pyogenicum of the lower lip, and gave a characteristic history of the condition. He said that a spot on his lip had bled one year previously, after which it healed perfectly and smoothly. Two weeks before he visited us it reappeared; after one week it bled profusely, and during the past four days had bled each day. It was curetted and cauterized with a silver nitrate stick, with subsequent uneventful healing.

CASE 8.—The only instance of two granulomas closely approximated on the red of the lower lip occurred in a man, 53 years of age. He said that six months previously a spot on the summit of the lower lip to the right of the median line bled copiously; since then it had not bled until a week before his visit to us. During this week, however, there had been four or five hemorrhages, principally at meals. The last hemorrhage he attributed to coughing; he coughed a great deal on arising. There were two lesions; one was 3 mm. in diameter, slightly prominent and a bright scarlet red but covered with a gray haze such as that which occurs in superficial streptococcic infection; the other was 2 mm. in diameter and was of the same bright red color as the other one but without the haze. When the lesions were curetted a comparatively large central blood vessel was exposed in the larger lesion. Both were curetted and cauterized with trichloracetic acid.

Some of these lesions exist for a long time without causing any trouble even in such an exposed and active position as the lower lip.

CASE 9.—As an example of this, a woman 55 years of age consulted us for a slightly prominent rounded lesion, capped by a black crust, which was situated on the exposed red part of the lower lip near the right corner of the mouth. It had recently bled twice. She thought the reason for the hemorrhages was the occurrence of a "cold sore" on it. On curetting it, we encountered a rather large blood vessel in the very center of the field. There was a small dot of black pigment on the exposed red part of the lower lip, midway between the median line and the left corner of the mouth, which was regarded as a nevus. The other lesion may also have been a nevus which later became infected. Nevus tissue, from its often vascular nature, might be more apt to proliferate in this way than normal tissue.

CASE 10.—A woman, 59 years of age, had what appeared to be a split papule in the left corner of the mouth which had appeared three months before she consulted us. A split papule in this situation always arouses the suspicion of syphilis, but no other syphilitic symptoms were present, and the papule remained unexplained for some time. Finally the lesion differentiated itself as two smooth lobules, an upper larger and a smaller lower one, with a smooth deep groove between them. The approximate surfaces were flattened by mutual pressure, and the neoplasm was perfectly soft. Microscopic examination showed the usual granulomatous tissue rich in blood vessels.

The patient had an excessive flow of very acid saliva. However, we could not connect this abnormality with the occurrence of the tumor. A good result was achieved by ablation and the use of silver nitrate and radium.

As previously noted, granuloma pyogenicum of the red part of the lip has a peculiar significance, as it invariably arouses the idea of cancer both in the patient and in the physician.

In the first place, it is necessary to reflect that granuloma pyogenicum may be either pedunculated or sessile, and that it may assume all the varities of appearance incident to exuberant granulation tissue. It may be clean and bright red, covered with pus or have a yellow or black crust, the latter from hemorrhage. However, it is most important to examine the surface immediately surrounding the base, as it is here that one may find evidences of epithelial infiltration either as a curb or as nodules proclaiming the lesion an epithelioma. The presence or absence of induration is also important; if it is present it may suggest either chancre or cancer.

The mode of operation on the lip also is of importance, as the smaller the scar the better. With the curet and the employment of a controllable caustic such as liquid trichloracetic acid, the least amount of tissue consistent with safety is removed, and an irradiation with radium or the roentgen rays is a further security against recurrence. As is well known, the scars after such an irradiation are smooth, pliable and inconspicuous. After the employment of nitric acid or the acid nitrate of mercury the scars are apt to be hypertrophic.

*Granuloma Pyogenicum of the Mouth.*—We have had an unusual number of cases of granulomata pyogenica of the mouth. This is at least partly explainable by association with a dentist who did a great deal of surgical work on the mouth and who was therefore especially interested in neoplasms in this cavity.

Case 11.—On June 29, 1922, a woman over 60 complained of a sensitive spot on the inside of the lower lip, which we touched with trichloracetic acid. One week afterward, we found a granuloma pyogenicum in this spot, which we treated by ablation and cauterization. It is a question whether we saw this lesion in its incipiency or whether our injury gave rise to the growth.

Case 12.—A man, 53 years of age, consulted us on account of a red spot in the center of the roof of the mouth, which he said bled at intervals. A red spot had appeared in this situation some time before, and had disappeared under treatment, the type of which he did not state. The lesion reappeared two months previous to consulting us. The surface of the small pea-sized tumor was peculiar in that it was dotted with minute red dots, evidently the loops of blood vessels. The whole surface of the hard and soft palate posterior to the tumor was laced with dilated capillaries. This tumor, also composed of dilated blood vessels, may have been part of the same process.

Case 13.—A woman, 35 years of age, had a pedunculated pea-sized tumor in the pouch of the right cheek, near the corner of the mouth. It was smooth and flattened on top, like a stone ground flat, and had a sharply bounded white edge surrounding a red center. There was also a lacework of lichen planus in this pouch. The patient thought that she had bitten the cheek until it bled, and ascribed the tumor to this injury; it had since bled at intervals. The lesion was

treated by ablation, caustic and radium. The lichen planus eruption would render the mucous membrane more liable to be bitten.

*Granuloma Pyogenicum of the Sole.*—A case of granuloma pyogenicum within the outer border of the sole of the left heel was of peculiar interest on account of a complicating circumstance.

CASE 14.—The patient, a girl, 15 years of age, was referred to us on Nov. 28, 1930, on account of a prominent, easily bleeding nub of bright red granulation tissue which was situated eccentrically in a field of dirty deep blue pigmentation so sharply delimited as to be remarkable. To make sure that the pigment was not on the surface, we wiped it with gasoline.

The patient said that four months previously she had noticed a black spot in this situation; she pricked it with a needle, and it disappeared. Intermittent bleeding, however, continued, and she consulted a physician, who cauterized it with a strong solution of silver nitrate. The growth recurred, together with the extended pigmentation. The granulation tissue did not have the rabbit flesh aspect so often seen in sarcoma, and no pigment was observable in the bright red mass itself. The pigmentation was remarkably sharply delimited, giving it an artificial appearance. The history of the primary black dot was so clear, however, that together with the extending pigmentation it forced us to think of sarcoma. Moreover, granuloma pyogenicum of the sole is a rarity. The lesion was well irradiated with heavily screened radium. Under treatment with irradiation and a salve the thick epithelium of the sole became sodden and raised from the subjacent tissues. Before sending the patient back to the surgeon who had sent her to us for irradiation, we trimmed back the overhanging tissue, and an interesting condition was revealed. All the pigment was found to consist of a slate blue mush adherent to the lower surface of the epithelial slab, and the pedunculated bright red granuloma stood out in a field entirely free of pigment. It was now clear what had happened. The lesion had lifted the epithelium so as to form a slitlike space, and along this space the silver nitrate had spread by capillary attraction and also by the pumping action induced by walking. The slate blue mush seen through the denser epithelium of the sole simulated tissue pigment, but looked more artificial. The history of a pigmented spot as an initial symptom and the occurrence of a slate blue pigmented field with an exuberant growth in it gave a fine mimicry of pigmented sarcoma, with the attendant grave prognosis. This lesion was subsequently excised by the surgeon.

## COMMENT

The analogies between granuloma pyogenicum and keloid are remarkable. Both are granulation tumors tending to organize into fibrous tissue; both frequently arise from traumatisms or apparently arise spontaneously; both grow to a certain size and then remain stationary; both tend to recur when removed, and when removed both tend to grow to the limit previously attained, and both are susceptible to actinic rays (roentgen rays or the gamma rays of radium). It must be said that although the tendency to recur in granuloma pyogenicum is definitely present, it is not nearly so inveterate as in keloid. In granuloma pyogenicum, if the field of elimination is sufficiently wide, the danger of recurrence is small, whereas in keloid the wider the field the

larger the recurrent keloid, and consequently the worse for the patient. This is one of the reasons for considering keloid an inherent condition of the tissues, consisting in an inclination to produce excessive granulation tissue and consequent hypertrophic scar tissue. In regard to the analogies, striking as they may be, we have never noted any tendency to formation of keloid after the removal of a granuloma pyogenicum, nor have we heard of such an occurrence. The analogies, however, as previously enumerated, are altogether too striking to be lightly cast aside.

## CONCLUSIONS

Although granuloma pyogenicum is such a simple tumor, consisting as it does of granulation tissue, it is worthy of separate consideration, both because it gives rise to so much anxiety on the part of the patient and because of its liability to recur, and therefore on account of its simulation of a malignant growth. It is also well to remember that though no further operation than curettage is necessary, this must be done thoroughly so as to include the blood vessels feeding the tumor as far down as the curet will go, that a caustic should be employed to go down still deeper, and that radium or roentgen treatment is also undoubtedly beneficial. Excision may also be employed, but subsequent treatment with the roentgen rays or radium is a further security against recurrence. The old axiom that the physician must not withhold from a patient any treatment that he considers beneficial should still be remembered.

# NORMAL PIGMENTATION OF THE ORAL MUCOSA

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Pigmentation of the oral mucosa is often considered an important diagnostic point in favor of Addison's disease. Its value in this respect is, however, diminished by the fact that it has been reported in other illnesses, such as acanthosis nigricans, vagabonds' disease, pernicious anemia, arsenic intoxication, chronic cachectic conditions due to tuberculosis, carcinoma and syphilis, scleroderma, exophthalmic goiter, von Recklinghausen's disease, hemochromatosis, malaria and pellagra. Moreover, oral pigmentation has been observed in many persons who on thorough examination showed no associated pathologic changes. This is especially true of Negroes. It has also been reported in such varied races as French (L. M. Bonnet,[1] Lortat-Jacob and Solente[2]), Filipino (Lortat-Jacob[3]), Algerian (Bonnet,[1] Brault and Montpellier[4]), Arabian, Chinese and East Indian (Reiche[5]), German (Jessner[6]), Gipsy and Roumanian (Sabaréanu[7]) and natives of Asia Minor (Combes[8]). Physiologic pigmentation of the oral mucosa is therefore not limited to any one race, but appears to be a common characteristic of the darker races. Even in oral mucous membranes that clinically showed no evidence of pigmentation Becker[9] demonstrated its presence microscopically in 74 per cent of his cases. It is also worthy of note that these persons were predominantly, if not exclusively, of German Swiss nationality and therefore not of a particularly dark type.

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From the Services of Drs. Williams, Bechet and Traub, the Stuyvesant Square Hospital, formerly the New York Skin and Cancer Hospital.

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In spite of the numerous references to oral pigmentation, knowledge of the subject is still meager because no systematic examination of a large number of persons has been made. The Negro in this country offers an admirable opportunity to study this question because of the wide variation of skin shades present in a large group.

## ORAL PIGMENTATION IN THE NEGRO

Observations were made on 220 Negroes of varying degrees of skin pigmentation and ranging in age from a few days to 65 years. The percentage of black pigment in the skin was determined with the pupil's color top,[10] a method that I have already used in a study of normal pigmentation of the nails in the Negro.[11]

To convey a rough idea of the shades represented by the figures obtained in this way, one may say that 35 per cent is a shade of tan; as the figure increases, the color becomes brown, with 70 per cent representing a dark brown, 80 per cent a brownish-black and 85 per cent a deep brownish-black.

The pigmented areas vary somewhat in appearance with their location. On the gums, in the lighter Negroes, they present as flat, light brown, irregularly circular areas, varying in size from 1 to 3 or 4 mm. in diameter and occupying approximately the center of the gum surface. In the darker subjects these pigmented areas are deeper in color, tend to become confluent and form a band encircling the central portion of the gum surface, as is well shown in figure 1. In very dark Negroes, those of 80 and 85 per cent skin pigmentation, not only the central portion but practically the entire gum surface may be covered with a pigmented plaque. In all cases there is a marked tendency for the pigmentation to be symmetrically bilateral. Microscopic examination of these pigmented areas shows a picture identical with that of skin pigmentation. The pigment is found chiefly in the basal cell layer with a tendency to occupy several layers of cells above the basal layer in the more darkly pigmented specimens. Often numerous chromatophores are seen in the papillary body.

On the hard palate and on the mucosal surface of the lips pigmentation may be diffuse, resulting in a general darkening of the entire area, or mottled, showing the presence of irregularly circular or elliptical areas of varying size, or a combination of both types may be seen. Very dark subjects show, as a rule, both diffuse and mottled areas, whereas the lighter Negroes usually have only mottling. On these surfaces there is also a tendency for the pigmentation to be symmetrically bilateral.

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10. Todd, T. W., and Van Gorder, L.: Am. J. Phys. Anthropol. **4**:244, 1921.

11. Monash, S.: Normal Pigmentation in the Nails of the Negro, Arch. Dermat. & Syph. **25**:876 (May) 1932.

On the soft palate pigmentation may also be either diffuse or mottled. In the latter case the pigmented areas are usually small and tend to surround the numerous small blood vessels in this structure.

Pigmentation on the cheeks is generally seen in the center, along what is usually considered to be the median raphé, as a flat brownish elongated area. The anterior third of this region is the area of predilection. In addition, mottled areas may be seen, and in very dark subjects a diffuse pigmentation of the entire cheek. Symmetry is also the rule here.

The tongue is unique in that there is no tendency for the pigmentation on the dorsum to be symmetrical. It is usually observed in the fungiform papillae in the anterior third. One or several of these may show pigmented summits with no other pigmentation observable elsewhere on the dorsum. In darker subjects the number of pigmented

Fig. 1.—Pigmented stripe on the upper gum surface in a Negro.

fungiform papillae increases. In very dark Negroes, those of 80 and 85 per cent skin pigmentation, pigmented plaques, varying in size from a few millimeters to a centimeter and more in diameter, are often seen. Both the fungiform and filiform papillae in these areas are pigmented. In older subjects the latero-inferior surface of the tongue occasionally shows a diffuse pigmentation. The plicae fimbriatae are often pigmented.

In the floor of the mouth pigmentation is usually limited to the areas about the orifices of the salivary ducts, and is generally seen as a pigmented circle surrounding the duct orifice.

*Oral Pigmentation and Age.*—At birth there is a relative paucity of pigmentation in the Negro, the skin of eighteen infants in the first week of life varying in pigmentation from 30 to 60 per cent as compared with a variation of from 45 to 85 per cent in the age group of 1 to 5 years inclusive. Oral pigmentation at birth is correspondingly slight. It was found to be present in six of the eighteen infants in

this series as light brown, irregular areas, usually over the palatal and lingual aspects of the gums in the upper and lower incisal regions, with a tendency toward bilateral symmetry. It is remarkable that in infants the pigmentation is first observed on the palatal and lingual surfaces and not on the buccal surface whereas in adult life the latter surface is very often found pigmented with the former surfaces free. This does not mean, however, that the palatal and lingual gum pigmentation observed in infants disappears in later life, as these children are usually the darker ones in whom pigmented areas will eventually develop on all portions of the gums.

In new-born infants oral pigmentation was observed only on the gums. This does not, however, exclude the possibility of other areas being occasionally pigmented in the darker infants. It does show that clinical pigmentation develops first on the gum surface.

The increased skin pigmentation occurring during the first few years of life is accompanied by increased oral pigmentation. In a 5 months old child with 75 per cent skin pigmentation, practically the entire gum surface, both internally and externally, was covered with pigmented areas. In another infant of 11 months with the same degree of skin pigmentation, there was, in addition to the pigmentation of the gum surface, a diffuse pigmentation of the hard palate, soft palate, lips and cheeks. After the age of 2 years practically complete encircling of the gums by a pigmented band is extremely common. At the age of 2½ and 2¾ years in two cases pigmentation of fungiform papillae on the tongue was observed. Pigmented plaques on the tongue comprising both the fungiform and filiform papillae appear to form much later, the earliest case being that of a boy aged 15 of 85 per cent skin pigmentation. Physiologic pigmentation of the oral mucosa in the Negro appears to be complete by the end of the second decade of life.

The same conclusion is reached by taking the darker Negroes, namely, those of 75, 80 and 85 per cent skin pigmentation in the various age groups, say, from birth to 9 years inclusive, from 10 to 19 inclusive and from 20 upward, and determining what percentage of the members of each of these age groups shows the following extensive pigmentation: complete encircling of the gums, upper and lower, buccally and lingually by a pigmented band, and pigmented areas on the hard palate, soft palate, cheeks, lips and tongue. Of the twenty-two subjects in the darker group between the age of a few days to 9 years inclusive, nine (41 per cent) showed the extensive pigmentation described; in the age group from 10 to 19 inclusive, twenty-two of forty (55 per cent), and in the group aged 20 or more years, thirteen of thirty-one (42 per cent). It is thus apparent that oral pigmentation is well on its way to completion by the end of the first decade and can be said to be practically complete

by the end of the second. Pigmentation occurring after the age of 20 can usually be traced to factors other than physiologic.

*Relationship of Oral to Cutaneous Pigmentation.*—Of two hundred Negroes, excluding new-born infants, ten (5 per cent) showed no pigmented areas in the mouth. With the exception of a subject with a skin pigmentation of 75 per cent, these ten were in the lighter group showing a skin pigmentation of less than 65 per cent. Every Negro with a skin pigmentation of 80 or 85 per cent showed considerable oral pigmentation.

The relationship of skin pigmentation to oral pigmentation can be shown even more strikingly by dividing the persons between the ages of 10 and 30 inclusive into two groups, those of a skin pigmentation of 70 per cent or less and those with a pigmentation of 75 per cent or more. Of the forty-nine in the first group, only four (8 per cent) showed a continuous pigmented band on all the gum surfaces, both upper and lower, buccally and lingually, extending from the molar region on one side to the molar area on the opposite side. Of the fifty-seven in the second or darker group, thirty-six (63 per cent) showed this extensive pigmentation of the gums and with it an increased pigmentation of other portions of the oral mucosa. The color of the pigmented areas was decidedly darker in those of deeper skin pigmentation.

*Areas of Predilection.*—It has already been shown that the gum surface is the first to show any signs of pigmentation. I am, of course, referring here to clinical and not to microscopic pigmentation. In many of the lighter Negroes pigmentation is observed, as a rule, only on the buccal aspect of the gum tissue in the region extending from the first bicuspid tooth on one side to that on the other side. With increased skin pigmentation the remainder of the gum surface becomes rapidly involved.

In this series the frequency of pigmentation of the various surfaces occurred in the following order: gum surface in 89 per cent of all cases, cheeks in 40 per cent, hard palate in 38 per cent, tongue in 33 per cent, lips in 30 per cent and soft palate in 26 per cent.

## PIGMENTATION IN OTHER RACES

Reference has already been made to the variety of races in which oral pigmentation has been observed. That it is by no means a rarity in races other than the Negro is shown by the fact that within a period of six months, while examining patients in a skin clinic who came in for other reasons, I observed thirty cases divided among the following races: Italian, Jewish, Greek, Roumanian, Chinese, Porto Rican, Syrian, Peruvian Indian, Hindu and Ceylonese (see table).

*Details of Thirty Cases of Oral Pigmentation*

| Case | Race | Age, Years | Sex | Pigment in Skin, per Cent | Areas Pigmented |
|---|---|---|---|---|---|
| 1 | American (Italian descent) | 19 | M | 55 | Gum tissue on buccal aspect in both upper and lower jaws, from first bicuspid tooth on one side to first bicuspid tooth on opposite side |
| 2 | Italian | 35 | F | 45 | Gum tissue on buccal aspect over upper right first bicuspid tooth |
| 3 | American (Italian descent) | 22 | M | 50 | Gum tissue on buccal aspect in upper jaw from second bicuspid tooth on one side to second bicuspid tooth on opposite side |
| 4 | Italian | 34 | M | 35 | Gum tissue on buccal aspect: in upper jaw over right first bicuspid and cuspid teeth; in lower jaw under right cuspid and lateral incisor teeth |
| 5 | Italian | 24 | F | 40 | Gum tissue on buccal aspect: in upper jaw over left central incisor tooth; in lower jaw in right molar region and under right bicuspid teeth and right central incisor tooth |
| 6 | Italian | 33 | M | 50 | Gum tissue on buccal aspect in both upper and lower jaws, from molar region on one side to molar region on opposite side |
| 7 | Italian | 22 | M | 45 | Gum tissue on buccal aspect: in upper jaw from second bicuspid tooth on one side to second bicuspid tooth on opposite side; in lower jaw from third molar tooth on one side to the third molar tooth on opposite side; a few fungiform papillae on left side of tongue anteriorly |
| 8 | American (Italian descent) | 22 | M | 40 | Gum tissue on buccal aspect: in upper jaw from second bicuspid tooth on one side to second bicuspid tooth on opposite side; in the lower jaw from the molar region on one side to the molar region on opposite side; pea sized areas in the center of both cheeks |
| 9 | Italian (fig. 2) | 25 | M | 60 | Gum tissue on buccal aspect: in upper jaw from second bicuspid tooth on one side to second bicuspid tooth on opposite side; in lower jaw from first bicuspid tooth on one side to first bicuspid tooth on opposite side; a few fungiform papillae on tongue |
| 10 | American (Italian descent) | 38 | M | 40 | Gum tissue on buccal aspect: in upper jaw over right and left central incisor teeth; in lower jaw from cuspid tooth on one side to cuspid tooth on opposite side |
| 11 | Russian Jewess | 25 | F | 50 | Gum tissue on buccal aspect: in upper jaw over central and lateral incisor teeth on both sides; in lower jaw below central and lateral incisor teeth on both sides |
| 12 | Russian Jew | 40 | M | 50 | Gum tissue on buccal aspect: in upper jaw over cuspid and first bicuspid teeth on both sides; in lower jaw from first bicuspid tooth on one side to first bicuspid tooth on opposite side |
| 13 | Roumanian Jew | 56 | M | 40 | Gum tissue on buccal aspect, over central and lateral incisor teeth on right side of upper jaw; hard palate in center over suture line |
| 14 | American Jew | 35 | M | 35 | Center of both cheeks and posterior corners of both sides of soft palate |
| 15 | Russian Jew | 67 | M | 40 | Center of both cheeks |
| 16 | Polish Jew | 39 | M | 40 | Gum tissue on buccal aspect in lower jaw under first bicuspid tooth; center of right cheek just back of corner of mouth |
| 17 | Russian Jew | 30 | M | 60 | Gum tissue on buccal aspect in both upper and lower jaws, from second bicuspid tooth on one side to second bicuspid tooth on opposite side; two fungiform papillae on tongue |
| 18 | Greek | 55 | F | 45 | Center of both cheeks |

*Details of Thirty Cases of Oral Pigmentation—Continued*

| Case | Race | Age, Years | Sex | Pigment in Skin, per Cent | Areas Pigmented |
|---|---|---|---|---|---|
| 19 | Roumanian | 46 | M | 45 | Gum tissue on buccal aspect: in upper jaw over central incisor and first bicuspid teeth on both sides; in lower jaw below left first bicuspid tooth. Outer portion of anterior fourth of soft palate on both sides. Center of both cheeks |
| 20 | Chinese | 41 | M | 40 | Gum tissue on buccal aspect in both upper and lower jaws, from first bicuspid tooth on one side to first bicuspid tooth on opposite side; outer portion of anterior fourth of soft palate on both sides |
| 21 | Chinese | 25 | F | 45 | Gum tissue on buccal aspect in both upper and lower jaws, from second bicuspid tooth on one side to second bicuspid tooth on opposite side |
| 22 | Porto Rican (no negroid features) | 30 | M | 55 | Gum tissue on buccal aspect in both upper and lower jaws opposite first bicuspid and lateral incisor teeth on both sides |
| 23 | Porto Rican (no negroid features) | 35 | M | 60 | Gum tissue on buccal aspect in both upper and lower jaws, from molar region on one side to molar region on opposite side |
| 24 | Syrian | 40 | M | 40 | Gum tissue on buccal aspect: in upper jaw over bicuspid and molar region on both sides; in lower jaw from molar region on one side to molar region on opposite side |
| 25 | Peruvian Indian | 30 | M | 60 | Gum tissue on buccal aspect: in upper jaw over right central incisor and lateral incisor teeth; in lower jaw from second bicuspid tooth on one side to second bicuspid tooth on opposite side |
| 26 | Hindu | 33 | M | 50 | Gum tissue on buccal aspect in both upper and lower jaws, from second bicuspid tooth on one side to second bicuspid tooth on opposite side; center of both cheeks |
| 27 | Native of Ceylon | 41 | M | 65 | Gum tissue on buccal aspect in both upper and lower jaws, from molar region on one side to molar region on opposite side; center of both cheeks |
| 28 | American (mixed Hindu and Roumanian parentage) | 20 | M | 75 | Gum tissue on buccal aspect in both upper and lower jaws, from molar region on one side to molar region on opposite side; gum tissue on lingual aspect in lower jaw, from molar region to cuspid tooth on both sides; center of hard palate over suture line; center of both cheeks |
| 29 | Brazilian Gipsy | 6 | F | 50 | Gum tissue on buccal aspect in both upper and lower jaws, from first bicuspid tooth on one side to first bicuspid tooth on opposite side; one fungiform papilla on left side of tongue anteriorly |
| 30 | Brazilian Gipsy (father of patient in case 29) | 35 | M | 55 | Gum tissue on buccal aspect in both upper and lower jaws, from first molar region on one side to first molar region on opposite side; center of both cheeks |

It is apparent from an examination of the table that there is no essential difference between physiologic pigmentation in the Negro and that in other races. The types of pigmentation and the areas of predilection are the same; one also observes the same relationship of mouth to skin pigmentation. Any differences between the various races are readily explainable by the variations in skin shades. One would not expect to see in the Italian or Jew the extensive oral pigmentation to be seen in the darkest Negro. When persons of similar shades of these races

are examined, however, there is no appreciable difference in the amount or the character of the oral pigmentation.

It is undoubtedly true that clinical oral pigmentation is present mainly in the more darkly pigmented races. This does not mean that the oral mucosa of these races alone possesses the power of pigmentation. The results of Becker,[9] already mentioned, demonstrating the presence of microscopic pigmentation in clinically unpigmented oral mucosa in 74 per cent of his cases tend to show that oral mucosa in general possesses this power. It varies in degree in different persons, increasing with increased skin pigmentation.

There is no essential difference in the processes of pigmentation in the skin and in the oral mucosa. The pigmentary changes in the skin accompanying or following inflammatory reactions, either the result of

Fig. 2.—Pigmented stripe on the upper gum surface in an Italian (case 9, table).

trauma or some diseased process, notably dermatitis herpetiformis, vagabonds' disease and lupus erythematosus, are familiar to all. It is also well known that the formation of pigment in these cases is much greater in persons of darker than in those of lighter skin color. Inflammatory reactions in the mouth similarly produce in many cases localized collections of pigment. They may be caused by trauma, such as the biting of the cheeks during mastication or the chemical trauma of tobacco smoke, or by disease processes. Lesions of lupus erythematosus in the mouth are often surrounded by a pigmented border in dark-skinned persons.

Recently Kistiakovsky [12] reported pigmented areas on the gums in a boy, aged 18 years, of Italian origin. They became somewhat lighter

12. Kistiakovsky, E. V.: Unusual Coloration of the Skin and the Mucous Membrane in Aryans, Arch. Dermat. & Syph. **24**:247 (Aug.) 1931.

in color for a time, but darkened considerably after the patient began to smoke a good deal and became constipated. To explain the pigmentation described, Kistiakovsky indulged in a rather fanciful theory that it may be due to an interaction of ether-sulphuric acids, resulting from constipation, and the metallic salts contained in tobacco smoke with the formation of metallic sulphuric combinations that dye the gum tissue.

There is no doubt in my mind that the case described by him is one of physiologic melanin pigmentation, showing an increased deposit of pigment under the irritative action of tobacco smoke. It has been shown how common this type of pigmentation is in Italians. The location and general outline of the pigmented bands coincides with those usually observed.

SUMMARY

1. The varied manifestations of physiologic oral pigmentation in the Negro are described.

2. It is practically complete by the end of the second decade of life.

3. It increases in intensity and amount with increased skin pigmentation.

4. Physiologic oral pigmentation in persons of other races is described; it is shown to be a common finding in dark-skinned persons and to differ in no essential respect from that observed in the Negro.

5. The likelihood of oral pigmentation being physiologic and not due to Addison's disease must always be kept in mind.

853 Seventh Avenue.

# News and Comment

**American Board of Dermatology and Syphilology.**—An "American Board of Dermatology and Syphilology" has recently been formed to certify those who are considered competent to practice this specialty. The purposes of the Board are identical with similar boards that have previously been formed by the ophthalmologists, otolaryngologists and obstetricians and gynecologists. The board consists of eight members, four of whom were elected by the American Dermatological Association and four by the Section on Dermatology of the American Medical Association. Provision is made for a rotation in membership by the annual election of one member from each of the two constituent organizations.

The personnel of the board is as follows:

Howard Fox, M.D., New York, President
W. H. Mook, M.D., St. Louis, Vice President
C. Guy Lane, Boston, Secretary
George M. MacKee, M.D., New York, Treasurer
Jay F. Schamberg, M.D., Philadelphia
Howard Morrow, M.D., San Francisco
Harold N. Cole, M.D., Cleveland
Arthur W. Stillians, M.D., Chicago.

At a later date an announcement of the time and place of examinations will be made.

# Abstracts from Current Literature

EDITED BY DR. HERBERT RATTNER

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METABOLIC STUDIES IN ADDISON'S DISEASE: THE EFFECT OF TREATMENT WITH THE CORTICAL HORMONE OF THE SUPRARENAL GLAND. C. H. GREENE, L. G. ROWNTREE, W. W. SWINGLE and J. J. PFIFFNER, Am. J. M. Sc. **183**: 1 (Jan.) 1932.

Cases of Addison's disease are usually not recognized until the stage of the definite clinical syndrome, asthenia, pigmentation, anorexia and loss of weight, is reached. If these patients are in good general clinical condition, there is usually slight reduction in the basal metabolic rate and blood sugar. In periods of crisis the effects of anhydremia and renal insufficiency change the chemical picture. The therapeutic use of the cortical hormone reduces the nausea and vomiting, thus aiding improvement in the usual clinical symptoms of the crisis.

THE SIGNIFICANCE OF THE COLLOIDAL GOLD REACTION AS A DIAGNOSTIC AND PROGNOSTIC AID IN NEUROSYPHILIS. F. G. NOVY, JR., Am. J. M. Sc. **183**: 401 (March) 1932.

In cases of latent and hereditary syphilis practically all patients examined had a negative or essentially negative reaction of the spinal fluid to the colloidal gold test. A few showed a color change as high as the "3" tube, but with very slight evidence of involvement of the central nervous system. The same findings applied to the group with congenital syphilis. Here also a small percentage showed changes in the fluid without positive clinical or other laboratory data.

In the group of primary and secondary syphilis most of the patients examined had evidence of some form of cerebrospinal involvement. Forty-nine showed a curve of the rather high middle zone, ten were negative, and eight gave a definitely paretic curve. The curve for sixty-five patients with dementia paralytica was found to be that usually recognized, with a maximum color change of "5"; nineteen had the same type of curve but less intense color changes; nine were considered to have a normal curve, and the same number had strong middle zone curves.

Tabetic gave a reaction of less intensity than paretic patients. Forty-two fluids gave reactions within normal limits; forty-seven had the typical tabetic middle zone curve, and eleven had paretic curves. The fluids in cases of the tabetic form of dementia paralytica were midway between those in tabes and paralysis. In diffuse cerebrospinal syphilis no characteristic curve was encountered, although the middle zone type was found most frequently.

Three chief methods of treatment were employed, intradural, tryparsamide and malaria, each producing an almost equal reduction in the color change in the colloidal gold reaction. With each method there was a group of patients with dementia paralytica who showed no change in curve or in color. The changes produced in the reaction following all methods of treatment were not uniform enough to be of prognostic significance. Changes in the spinal fluids were often found in patients receiving no treatment.

JAMIESON, Detroit.

MYCOSIS FUNGOIDES. B. MARKOWITZ, Am. J. Surg. **16**:113 (April) 1932.

Two cases are reported, one of mycosis fungoides and the other of Hodgkin's disease. An analysis of the clinical histories and pathologic studies render support

to the infectious character of these entities rather than the neoplastic. The pathologic picture, present in each case of lymphocytic infiltration with plasma cells and fibroblasts, without destructive character or invasive tendency, in the author's opinion, supports the concept of an infectious origin.

RATTNER, Chicago.

DISPENSARY TREATMENT OF SYPHILIS. H. H. HAZEN, Am. J. Syph. **16**:1 (Jan.) 1932.

This is a timely article. Dr. Hazen warns especially against the unnecessary duplication of clinics in the larger cities, which leads to insufficient personnel, poor attendance on the part of physicians and patients and poor results. He thinks that university clinics are urgently needed and makes a plea for a paid staff. He suggests that the Wassermann and Kahn tests be done in fewer laboratories in order to reduce the cost, and that the clinics cease to be free testing places for new and untried antisyphilitic remedies.

SOME OBSERVATIONS ON THE TREATMENT OF SYPHILIS. H. N. COLE, Am. J. Syph. **16**:9 (Jan.) 1932.

Dr. Cole presents a general résumé of the various antisyphilitic remedies in use at the present time. Despite their tendency to neglect mercury in favor of bismuth, physicians should not forget its value. When the quick action of mercury is desired, Cole uses one of the soluble mercury salts, injections being given daily. He also uses mercury salicylate and mercury inunctions where gradual absorption and excretion of mercury are desired. He concedes that bismuth is a remedy probably superior to mercury. He gives the insoluble salts once a week and the soluble bismuth preparations twice a week. He questions whether the liposoluble bismuth preparations on the market have any advantage over the other bismuth products.

Arsphenamine, he believes, is still the most potent antisyphilitic remedy. He has discarded sulpharsphenamine because of its propensity to produce a severe reaction. Tryparsamide he employs in neurosyphilis, especially after malaria therapy.

Cole believes that continuous therapy is the rational mode of treating patients with syphilis and advocates its adoption by every conscientious physician. He presents a brief outline regarding treatment of seronegative and seropositive early syphilis. Cole employs malaria therapy for any resistant syphilis of the central nervous system. Following malaria, he uses arsphenamine or tryparsamide. As a conclusion, there is a discussion as to whether syphilis is on the decline or increase.

REACTIONS FOLLOWING THE ADMINISTRATION OF THE ARSPHENAMINES AND METHODS OF PREVENTION. F. A. IRELAND, Am. J. Syph. **16**:22 (Jan.) 1932.

Of 2,100 patients who had received arsphenamine therapy, 11.2 per cent had various symptoms of intolerance to arsphenamine. The proportion of reactions was approximately twice as great in female as in male patients, and old arsphenamine was responsible for a higher percentage of reactions. Gastro-intestinal reactions were the most common type encountered. Of all the reactions, 72.5 per cent occurred early in treatment, between the first and tenth injections. High dosage, rapid injection and insufficient dilution of the arsphenamine tended to produce more frequent and severe reactions. Atropine sulphate, epinephrine, ephedrine, calcium gluconate and the Besredka technic were useful means of preventing reactions. The pathogenesis of nearly all types of reactions is obscure and awaits further elucidation.

IODINE POISONING AND IODISM FROM LIPIODOL. D. A. CARMICHAEL, Canad. M. A. J. **26**:319 (March) 1932.

Two cases are reported in both of which the cutaneous manifestations consisted of wheals and hemorrhagic bullae. Lesions appeared on the skin and the mucous membranes of the mouth. Iodized poppy-seed oil 40 per cent was injected into the bronchi in each instance.

RATTNER, Chicago.

TULAREMIA. MARGARET FOULGER, ALFRED M. GLAZER and LEE FOSHAY, J. A. M. A. **98**:951 (March 19) 1932.

A case of tularemia is reported in which auto-inoculation of two fingers of the left hand by contact with the primary lesion on the index finger seems highly probable; the use of convalescent serum was without beneficial effects; lesions of the peritoneum, both focal and diffuse, are described for the first time, and a new staining method revealed the presence of Bacterium tularense in tissue sections from certain of the involved organs.

AUTHORS' SUMMARY.

THE RELATION OF HYDROSTATIC PRESSURE TO THE GRADIENT OF CAPILLARY PERMEABILITY. P. D. MCMASTER, S. HUDACK and P. ROUS, J. Exper. Med. **55**:203 (Feb.) 1932.

From the evidence of their experiments the writers believe that there are local differences in the walls of the vessels to account for the gradient of permeability found in the capillaries of voluntary muscles and in the capillaries and venules of the skin. They also found that this gradient was influenced by hydrostatic conditions, yet existed independent of them.

THE VESSELS INVOLVED IN HYDROSTATIC TRANSUDATION. P. D. MCMASTER and S. HUDACK, J. Exper. Med. **55**:417 (March) 1932.

When venous pressure is moderately increased, the permeability of the cutaneous capillaries and venules is accentuated, producing a transudation leading to edema. When the venous pressure approximates the arterial pressure, the capillaries near the arterioles also become more permeable. When this occurs, the capillaries and venules everywhere leak fluid.

THE GRADIENT OF PERMEABILITY OF THE SKIN VESSELS AS INFLUENCED BY HEAT, COLD AND LIGHT. S. HUDACK and P. D. MCMASTER, J. Exper. Med. **55**:431 (March) 1932.

Mechanical, electrical, thermal and clinical stimuli all produced practically the same response in the cutaneous vessels, with the result that the staining phenomena to determine permeability were also practically identical.

JAMIESON, Detroit.

STREPTOCOCCIC STOMATITIS. S. V. MEAD, Mil. Surgeon **70**:238 (March) 1932.

Three cases are described of an entity that is usually mistaken for Vincent's ulceromembranous stomatitis. It occurs following a streptococcic sore throat or as a result of poor oral hygiene, especially in a patient with a dietary deficiency. The disease starts with gingivitis about a tooth, which spreads and progresses until the gingivae are hypertrophied and congested, bleed easily and are painful. The gums do not ulcerate unless there is a superimposed Vincent's infection. The infection usually responds well to treatment, which consists of irrigations with warm solutions of salt, soda and the recognized antiseptics, a diet rich in vitamins, with large quantities of orange juice, and correction of primary factors, such as diseased tonsils or teeth.

RATTNER, Chicago.

THE MICROSCOPIC SLIDE PRECIPITATION TEST FOR SYPHILIS WITH SPINAL FLUID. JOSEPH JORDAN ELLER and CHARLES ROBERT REIN, New York State J. Med. **32**:71 (Jan. 15) 1932.

The paper presents a comparative study of the microscopic slide precipitation test for syphilis with spinal fluids with the Wassermann reaction, Kahn test, albumin-globulin ratio and colloidal gold reaction. The following conclusions were reached: 1. The microscopic slide precipitation test with spinal fluids has been found to be more sensitive than the Wassermann reaction, modified Kahn test, colloidal gold reaction and albumin-globulin ratios. 2. This test gave results that agreed more frequently with the clinical condition of the patients than those of the other tests of the spinal fluid used in this series. 3. The test is simple, and the results magnified by the microscope are read accurately with ease.

DIAGNOSIS AND TREATMENT OF SYPHILIS. A. B. CANNON, New York State J. Med. **32**:316 (March 15) 1932.

The various stages of syphilis are briefly reviewed, special emphasis being placed on the more common diagnostic errors. The routine treatment is well summarized. When syphilis attacks special areas, such as the mucous membranes of the mouth, the dangers of complicating carcinoma are pointed out. The value of a biopsy to make certain of the diagnosis in the presence of a 4 plus Wassermann reaction is emphasized in doubtful cases. Interesting cases of osseous and vascular syphilis and of neurosyphilis are cited to illustrate diagnostic errors.

TRAUB, New York.

SOME INTERESTING DRUG ERUPTIONS. H. HALDIN-DAVIS, Brit. M. J. **1**:423 (March 5) 1932.

In speculating as to the nature of the factor producing susceptibility, the author likes to believe that susceptibility to drug eruption depends on some chemical peculiarity of the protoplasmic molecule of the subject; that there is a characteristic chemical formula for the protoplasm of every person, but there will be slight individual variations in the chemistry of the protoplasmic molecule. The side chains of the protein molecules will have different unsatisfied affinities on which the susceptibility of the person to various drugs may well depend. The remainder of the paper is given to a consideration of the practical aspects of the subject. The author describes cutaneous manifestations caused by iodine, bromine, arsenic, silver and gold. Gold can cause a pruritic follicular rash, pustular eruptions on the scalp, severe ulcerations of the tongue and pharynx or a generalized exfoliative dermatitis. The paper is a short one, and the subject is only briefly considered.

HERPES ZOSTER INVOLVING THE URINARY BLADDER. CLEMENT C. CHESTERMAN, Brit. M. J. **1**:563 (March 26) 1932.

A woman with herpes zoster affecting areas innervated by the second and third sacral roots complained of intolerable irritation and frequency of micturition. In the absence of any other cause, it was thought that the urinary symptoms were due to involvement of the urinary bladder by herpes zoster. There was an epidemic of chickenpox in the community. The author was able to find references to only three cases of herpes zoster of the bladder.

RATTNER, Chicago.

SERODIAGNOSIS OF ACTIVE SYPHILIS BY MEANS OF SERUM AUTO-ANTIGEN (S. R.). O. SCIARRA, J. Trop. Med. **35**:49 (Feb. 15) 1932.

A minute description is given of the preparation of all the reagents used in this test and of the exact method of procedure in its performance.

JAMIESON, Detroit.

SOME OBSERVATIONS ON THE PATHOGENESIS OF ECZEMA OF INTERNAL ORIGIN AND OTHER ALLERGIC DISEASES. G. H. ORIEL, Proc. Roy. Soc. Med. **24**:1171 (July) 1931.

Over 200 cases of eczema of internal origin and of other allergic diseases were investigated with particular reference to specific sensitization. It was found that a fair percentage of patients were sensitive (by the intradermal method) to their own urinary proteose. The proteose (not a true proteose but so-called for the sake of brevity) is isolated from the urine by acidulating the urine, shaking it with a quarter of its volume of ether, and treating the ether suspension with an excess of alcohol after it has separated. The resulting precipitate is centrifugated off, suspended in distilled water and again centrifugated. The residue is soluble in dilute alkalis. When isolated and injected intradermally into a sensitized person, a reaction results similar to that seen after injection of an antigen to which an allergic patient is sensitized. Desensitization was attempted by the injection of minute quantities of the proteose with good results in some cases.

CHRYSANTHEMUM DERMATITIS. H. MACCORMAC, Proc. Roy. Soc. Med. **25**:391 (Feb.) 1932.

A woman aged 26 years, first observed an eruption on the face twelve years prior to examination; this had recurred annually, with the exception of one year when she changed her occupation from that of a country domestic to that of a shop assistant in a town. The hands had never been affected. When the patient was first seen in the outpatient department her face was markedly swollen and edematous. The appearance of the eruption and the history pointed to an external agent, probably chrysanthemums, with which it was found she had been in contact. She was admitted to the hospital, and when the condition had subsided chrysanthemum petals were rubbed into the skin on one side of the face, and chrysanthemum leaves on the other. The result was a return of the eruption in acute form on the next day. Later, some of the actual plants from the house in which she was employed were obtained, and when these were applied to the scapular region on the right side a pronounced flare-up on the face and slight dermatitis of the shoulder occurred.

Graduated injections of the essential oils that exist in the leaves in proportions varying from 0.01 to 0.1 per cent were first considered as a method of desensitizing the patient in this case. Later a simpler method was devised, viz., rubbing the plant into the skin through measured areas cut in scale in stiff paper. An increasing dose of the antigen can thus be accurately given. For this purpose the thigh was selected since, in this location the reaction had not been unduly severe.

GUY, Pittsburgh.

ERYSIPELOID. G. BELGODERE, Ann. de dermat. et syph. **2**:1241 (Dec.) 1931.

A case of erysipeloid is reported, the literature is reviewed, and the subject is thoroughly covered from the standpoints of etiology, pathogenesis, immunobiology, clinical characteristics and therapy. The article can be recommended as probably the best monographic treatment of the subject to date. The effort was inspired by the fact that in France erysipeloid is "a dermatosis little known because it is rare, rare because it is little known."

GANDY, Houston, Texas.

THE CUTANEOUS TUBERCULIN REACTION IN MAN AND ANIMAL BY MEANS OF THE TUBERCULIN STAMP TESTS. PHILIPPE KFOURI, Bull. et mém. Soc. de méd. de Paris, Dec. 11, 1931, p. 615.

In his work with tuberculin in man and animals, the author came to the conclusion that the clearness and the precision of a tuberculin reaction depends, all

other factors being equal, on sufficient time of contact of the tuberculin with the skin and, consequently, on the efficient impregnation of the skin with the toxin. This realization made him introduce, in 1928, the method of "tuberculin stamp tests"; tiny squares of sterilized blotting paper are imbibed with undiluted old tuberculin Koch and preserved aseptically in glass tubes that are protected from air and light. These stamps are applied in men to the intact skin (epidermo reaction), to the scarified skin (cuti reaction) or to the slightly scratched skin (dermo reaction), and fixed by means of adhesive paper and bandage. The time of contact for the first two reactions is two hours, and for the last reaction, five or six hours.

The results obtained by this method are most satisfactory. The local reactions are clear and precise. Of advantage are also the simple technic and the rapid and aseptic manipulation.

BLOOM, New York.

FREQUENCE OF "TRICHOPHYTON RADIOLATUM" IN DERMATOPHYTOSIS OF THE FEET. J. DUCHE, Bull. Soc. franç. de dermat. et syph. **39**:160 (Jan.) 1930.

In forty-one patients suffering with dyshidrosiform eruptions of the feet, Trichophyton radiolatum was isolated in twenty-five, or 76 per cent.

DARIER'S DISEASE WITH CLINICALLY ATYPICAL LESIONS. GOUGEROT and OLGA ELIASCHEFF, Bull. Soc. franç. de dermat. et syph. **39**:163 (Jan.) 1932.

The patient had folliculopapular lesions on the trunk which were clinically and microscopically typical of Darier's disease, and in addition harmless looking papillomatous and verrucous lesions on the backs of the hands and on the chest. The presence of the latter element in the picture made a clinical diagnosis of atypical Darier's disease seem tenable. Yet microscopic examination of these lesions, which so closely resembled those of verruca vulgaris, showed the characteristic dyskeratotic changes of Darier's disease the same as did those that were clinically typical of the disorder.

TWO CASES AND SOME CONSIDERATIONS OF ACANTHOSIS NIGRICANS. HOULOUSSI BEHDJET, Bull. Soc. franç. de dermat. et syph. **39**:192 (Jan.) 1932.

Up to 1932, 221 cases of acanthosis nigricans had been recorded in the literature. Two others are presented here. Only about one third of the cases reported have been accompanied by a visceral neoplasm. Thus the majority have been of the benign type. So far as the cutaneous manifestations are concerned, the morphologic and histologic dissimilarities between the benign and malignant forms of the disease are too slight to be of any aid in differentiating between them. The older the patient, the greater is the probability of malignancy. The condition predominates in women. The differential diagnosis usually entails a consideration chiefly of Darier's disease and of Fox-Fordyce's disease.

KERATOSIS PALMARIS ET PLANTARIS CURED WITH MAGNESIUM. JEAN LACASSAGNE, LIÉGEOIS AND FRIESS, Bull. Soc. franç. de dermat. et syph. (Réunion dermat. de Lyon) **39**:8 (Jan.) 1932.

A man, aged 22, was afflicted with keratoderma of the palms and soles, dating from infancy. His mother had the same condition. The hyperkeratotic layer on both hands and feet was 1 cm. thick, and was traversed by deep furrows. The patient had never been able to do manual labor, and even walking was painful. His general health was good. In view of the known beneficial action of magnesium on veruccae, he was given 0.4 Gm. of calcined magnesium per day. (Calcined magnesium has the property of transforming rapidly in the stomach into magnesium chloride). After one week there was considerable improvement. In two weeks the lesions had disappeared from the hands, save for a small hyper-

keratotic plaque on each hypothenar eminence. On the twenty-fourth day the hands were normal, and the feet were normal except for a small patch on each heel. Treatment was stopped, and there had been no recurrence within thirty days.

In the discussion Pillon stated that he had treated in like manner, with considerable benefit, a tabetic patient who had a perforating ulcer and marked keratoderma of the plantar surfaces. Carle spoke of a case similar to the one presented, claiming that after magnesium given *per os* had failed, the condition responded to local application of a pomade consisting of equal parts of calcined magnesium and liquid petrolatum. Lebeuf observed that he had seen two patients with hyperkeratotic eczema in whom the hyperkeratotic element disappeared under magnesium therapy.

CYLINDROMA OF THE FACE AND SCALP. J. NICOLAS, G. MASSIA and F. LEBEUF, Bull. Soc. franç. de dermat. et syph. (Réunion dermat. de Lyon) **39**:10 (Jan.) 1932.

A woman, aged 34, presented multiple growths of the face and scalp. The first one appeared at the age of 17. They were rounded, rosy, hard tumors from the size of a pinhead to that of a lentil, covered with a fine scale, both discrete and fusing to form lobulated masses. They occupied the chin, the upper lip, the sides of the nose and the temples, and were disseminated throughout the scalp. The histologic structure bore a close resemblance to that of basal cell epithelioma. The condition was a classic example of benign cylindroma.

NITRITOID CRISIS FOLLOWING BISMUTH. J. NICOLAS and F. LEBEUF, Bull. Soc. franç. de dermat. et syph. (Réunion dermat. de Lyon) **39**:82 (Jan.) 1932.

Two cases are reported in which a nitritoid crisis developed after the intramuscular injection of bismuth, a rare phenomenon. The preparation used was bismuth hydroxide in oil suspension. In one patient the reaction appeared after the second injection, and was followed by gingivitis and stomatitis. The other patient had been taking bismuth intermittently for six years, and he subsequently showed no signs of bismuth intolerance, such as albuminuria or stomatogingivitis.

GANDY, Houston, Texas.

LYMPHOGRANULOMATOSIS. TITU VASILIU et al., Presse méd. **40**:25, 1932.

This is the report of a session of the Société anatomique devoted to lymphogranulomatosis. The disease is generally accepted to be an infectious granuloma, but the tuberculous etiology is rejected. Bezançon reports that inoculations of tissue into animals have occasionally given rise to generalized adenopathies transmissible in series. The lymph nodes contained many eosinophils, but no organisms could be detected. Cornil in the same manner obtained reticular changes and microscopic abscesses in the spleen, which appeared after intervals of three, four and nine months. The wide variations in the histologic picture of Hodgkin's disease are emphasized, pseudoneoplastic, inflammatory and plasmocytic forms being described. All of the cell forms are traced to the hemohistioblast of Ferrata. Some authors have attempted to identify the Reed-Sternberg cell with the megalokaryocyte of the marrow on the basis of the morphology and the high platelet count. No essential distinction is believed to exist between the typical form of the disease and those showing extensions to the lungs and pleura, the bones and the skin. The spleen is involved in 95 per cent of the cases. Henschen calls attention to certain rare generalized hyperplasias of the reticulo-endothelial system that defy interpretation. They have been termed histiocytosis, endotheliosis and reticulosis.

A. F. DEGROAT. [ARCH. PATH.]

NEW TREATMENT FOR VARICOSE ULCER. L. BIANCALANA, Boll. e mem. d. Soc. piemont. d. chir. **1**:1233 (Dec. 19) 1931.

Biancalana states that the new treatment consists in the use of a rubber bath-sponge applied to the varicose ulcer so as to produce a marked elastic compression. The ulcer is first cleansed thoroughly. A slight cauterization is done with a silver nitrate solution. A thin layer of zinc oxide ointment is then applied, and the ulcer is covered with gauze. The rubber sponge must be of good quality and rather hard, and must overlap the ulcer by more than 2 cm. The sponge is held in position with a compressive bandage with a semi-elastic band, which is wrapped about the whole leg up to the knee. The patient, with this bandage, can continue to follow his occupation; in fact, he should walk a great deal, to provoke the rhythmic contractions of the musculature, thereby aiding the circulation. The patient may feel some discomfort, which will disappear on walking about. The treatment is contraindicated in patients subject to attacks of phlebitis and also in patients confined to bed. In the ten patients treated the results were favorable and rapid, and thus far there have been no recurrences.

EDITOR'S ABSTRACT [J. A. M. A.]

PAROXYSMAL HEMOGLOBINURIA A FRIGORE. L. CATTANEO, Gior. ital. di dermat. e sif. **72**:1159 (Oct.) 1931.

This lengthy article is a résumé of the present-day knowledge of paroxysmal hemoglobinuria, particularly the a frigore type, which the author claims is always due to syphilis. He reports a case in detail in which specific treatment achieved a definite cure.

PSEUDOPELADE BROCQ. F. Lisi, Gior. ital. di dermat. e sif. **72**:1249 (Oct.) 1931.

The author reviews the literature from Newman, in 1868, who seems to have been the first to write about this condition, to Brocq, who in 1885 and 1905 separated it as a clinical entity. He reports two cases, bringing the total published to date to 168, of which 18 were reported in America. No pathogenic fungi or bacteria were found in his cases, after repeated cultural attempts. Pathologically, there were atrophy of the skin, slight inflammatory infiltration of the small lymphocytes around the vessels and hair follicles and atrophy of the sebaceous glands.

PRINGLE'S NEVUS: A CONTRIBUTION TO THE STUDY OF SYMMETRICAL FACIAL NEVI. V. NICOLETTI, Gior. ital. di dermat. e sif. **72**:1278 (Oct.) 1931.

This is the second case reported by the author. The patient was a boy, aged 14, who had no history of nervous disease. There were about seventy small, prominent, papular lesions on the face, which were the color of normal skin or perhaps slightly darker, of firm consistency and about the size of a pinhead. Histologically, there were fibrosis, diminution of the elastic fibers, ectatic blood vessels and cellular collections composed of epithelioid cells and fibroblasts. Cellular nests of nevic cells were present in most sections, which were derived from the epidermis.

A STUDY OF THE BLOOD IN LEPROSY. PINO PINETTI, Gior. ital. di dermat. e sif. **72**:1319 (Oct.) 1931.

The author examined the blood in thirty-one cases of leprosy. He found slight anemia, a normal leukocyte count and a strong deviation of the Arneth formula to the right. The blood groups, according to the author, have no relation to leprosy.

A Case of Dermatitis Herpetiformis with Symptoms of Epidermolysis Bullosa. Enzo Bizzozero, Gior. ital. di dermat. e sif. **72**:1397 (Dec.) 1931.

The patient was a man, aged 36, with a typical dermatitis herpetiformis that presented two peculiarities worthy of mention. One was the presence of atrophic scars with numerous milium cysts; the scars had caused the loss of all the toenails. The other was the formation of large bullae on the hands and the feet, occasioned by slight traumas, such as rubbing with the fingers. Hyperhidrosis was present. The condition seemed to be due to latent edema of the dermo-epidermal junction.

Pemphigus and the Glands of Internal Secretion. G. Chiale, Gior. ital. di dermat. e sif. **72**:1405 (Dec.) 1931.

The author reports the clinical and necropsy observations in ten cases of pemphigus. His studies were directed to find the possible etiologic relationship between disturbances of the glands of internal secretion and pemphigus. Careful examination of the pineal gland, hypophysis, suprarenals, pancreas, testes, ovaries, heart, liver and kidneys failed to disclose definite lesions bearing any relationship to the cutaneous condition.

Darier-Roussy Sarcoid. Mario Artom, Gior. ital. di dermat. e sif. **72**:1464 (Dec.) 1931.

The author reports a case of subcutaneous sarcoid of Darier-Roussy in a man, aged 27, suffering from pulmonary tuberculosis. He discusses the importance of tuberculosis in the etiology of the sarcoids, and, having noted how sarcoids react locally to the intradermal injection of tuberculin, he concludes that sarcoids are possibly a mode of reaction of the skin in persons with increased cutaneous reactivity to the toxins of tuberculosis.

Purpura Annularis Telangiectodes, Majocchi. Luigi Ciarrocchi, Gior. ital. di dermat. e sif. **72**:1525 (Dec.) 1931.

The author presents a review of the literature, with general considerations of the etiology, pathogenesis, histology and evolution of the disease. He reports two cases that had been observed repeatedly for a number of years. He concludes that purpura annularis telangiectodes is in some way intimately related to tuberculosis and to suprarenal insufficiency.

Xeroderma Pigmentosum. Luigi Ajello, Gior. ital. di dermat. e sif. **72**:1600 (Dec.) 1931.

This is a necropsy report of a case of xeroderma pigmentosum with a large ulcerated carcinoma of the face. The histologic lesions of the skin are described in detail. The most important visceral lesions were degeneration and sclerosis of the ovaries and the thyroid gland, hyperplasia of the suprarenals, particularly of the medullar substance, and chronic nephritis.

A Rare Location of Hypoderma Bovis in Man. Ribeiro dos Santos, Gior. ital. di dermat. e sif. **72**:1624 (Dec.) 1931.

The patient was a Brazilian farmer who presented two nodosities on the dorsum of the penis, from which the author extracted two larvae of Hypoderma bovis. This condition is frequently found in cattle in Brazil.

Pardo-Castello, Havana, Cuba.

GENESIS AND MODE OF SPREADING OF ERYSIPELAS CARCINOMATOSUM. W. BRACKERTZ, Arch. f. clin. Chir. **169**:82 (Jan. 21) 1932.

Brackertz names various forms of cancer of the breast and then directs attention to the form that Küttner designated as erysipelas carcinomatosum. On the basis of a case history he demonstrates that the subepidermoidal spreading of the carcinoma in erysipelas carcinomatosum (Küttner) takes place primarily by the lymphatic route in the corium of the skin. When cases are reported in which carcinomatous thrombi are found in the capillaries of the skin, these are the result of secondary perforation into the vessel, after the carcinoma has already spread into the lymphatics of the skin. The question why in these cases the carcinoma spreads by way of the lymph channels of the skin is explained thus: If the deeper drainage channels have been blocked either by cancerous infiltration or by surgical division (amputation of mamma) the cancer process must follow the lymph channels of the skin. It is assumed that the inflammatory hyperemia in the corium, which causes the redness of the skin, is a reaction of the host tissue to the invading foreign carcinoma cells, for a bacterial cause of the erysipelas-like redness of the skin could not be detected. It is also demonstrated that the cancer infiltration reaches beyond the area of redness into the apparently healthy skin. This factor is considered the main cause of the unfavorable operative prognosis.

EDITOR'S ABSTRACT. [J. A. M. A.]

BLUE NEVUS. RUDOLF BEZECNY, Arch. f. Dermat. u. Syph. **164**:314, 1931.

The blue color of a nevus is usually due to the fact that the melanoblastic cells are present deep in the corium and are separated from the epidermis by a pigment-free epidermis. The author describes a case that was clinically one of a blue nevus but showed an entirely different microscopic picture. The nevus consisted of a combination of colorless nevus cells interspersed with numerous chromatophores containing both melanin and hemosiderin. Practically the entire cutis was occupied by the nevus. The mass had originally been brown but had become bluish after an attempt had been made to remove some of the hairs by electrolysis. The latter procedure had probably produced some hemorrhage, followed by the formation of hemosiderin, which was undoubtedly a factor in the production of the bluish tinge.

CLASSIFICATION AND NOMENCLATURE OF ATROPHY AND SCAR-PRODUCING ALOPECIAS AND FOLLICULITIS. ERICH HOFFMANN, Arch. f. Dermat. u. Syph. **164**:317, 1931.

Hoffmann, in a well illustrated article, divides atrophy and scar-producing alopecias and folliculitis into six groups: (1) alopecia atrophicans areolata (Brocq's pseudopelade), which leads to scar formation without visible folliculitis; (2) folliculitis decalvans cicatrisans capilitii (acné décalvante of Lailler and folliculité épilante of Quinquaud), in which small areas, usually on the vertex, are affected showing central scarring and peripheral folliculitis; (3) perifolliculitis capitis abscedens et suffodiens cicatrisans, showing deep undermining abscesses ending in scarring (this condition is related to acne conglobata cutis); (4) folliculitis sycosiformis atrophicans capilitii, which affects the temples and the areas behind the ears symmetrically and is characterized by central scarring and peripheral folliculitis; (5) folliculitis sycosiformis atrophicans barbae (Brocq's sycosis lupoïde and Unna's ulerythema sycosiforme), showing oval symmetrical areas on both sides of the face in the bearded areas, with central scarring and peripheral folliculitis; (6) folliculitis sycosiformis atrophicans (cutis lanuginosae) corporis, usually found on the legs of men, showing large areas with central scarring and peripheral folliculitis.

CLINICAL PICTURE AND PATHOGENESIS OF BROMODERMA VEGETANS. BRUNO BLOCH and F. TENCHIO, Arch. f. Dermat. u. Syph. **165**:93, 1932.

A severe case of acneform and vegetating bromoderma is described in a woman after a total intake of 17.6 Gm. of potassium bromide by mouth. The case is noteworthy, first, because of the long period of latency, namely, six months from the last dose of the bromide to the appearance of the cutaneous lesions; second, because of the progressive character of the lesions, and, third, because of the involvement of the mouth (vegetating bromoderma of the oral mucosa and tongue) and of the blood (leukocytosis, marked eosinophilia and anemia).

Intravenous saline therapy was of no avail, and the patient died. Autopsy showed the cause of death to be thrombosis of the transverse sinus and embolus in the pulmonary artery.

With the Belote method bromine was shown to be present: (*a*) in the urine almost every day for the first six months, and toward the end more seldom and less markedly. (*b*) in the organs, post mortem, most marked in the thyroid and in the spontaneously formed efflorescences of the skin and mucosa, weak in the artificially produced lesions and in the rest of the skin, submucosa, suprarenals and spleen, hardly at all in the liver and ovaries, and not at all in the kidneys.

It was possible to produce on apparently normal skin lesions that were clinically and histologically identical with those that had formed spontaneously. A positive result was obtained with inorganic bromine in the form of bromides, and with organic bromine as eosin, potassium iodide and sodium fluoride, while organic and inorganic bound chlorine had no effect. Positive results were also obtained with nonhalogens that produced a strong primary inflammatory reaction, such as sodium carbonate, with cantharides plaster and with traumatism in the form of an incision. The substances mentioned were applied in the same manner as patch tests.

Bromoderma is considered to be an idiosyncratic condition of the skin, mucosa and internal organs, and is brought about by sensitization. As antigens must be considered not only the bromide directly ingested but also that retained in the organism in the form of bromine protein compounds. The antigenic action of the retained bromine explains the latency and late progression. The sensitization is present not only in the mesodermal portions but in the epithelial layers of the skin and mucosa. The formation of bromoderma lesions by strong banal irritants is explained by the pouring out of bromine into an inflamed and injured area similar to a Köbner phenomenon in hematogenous infections, such as vaccinial and trichophytic infections and tuberculosis.

MONASH, New York.

THE ANGIOLUPOID OF BROCQ-PAUTRIER. FRANZ PREISS, Dermat. Wchnschr. **93**:1809 (Nov. 21) 1931.

A case of angiolupoid is described in a woman, aged 34, who suffered from diabetes mellitus. During the course of observation, xanthelasma and intertrigo of the genitals developed. Hyperglycemia is considered an etiologic factor in the development of angiolupoid. No evidence of tuberculosis or syphilis was found.

THE MECHANISM OF THE CURE OF WARTS BY SUGGESTION. J. SAMEK, Dermat. Wchnschr. **93**:1853 (Nov. 28) 1931.

The author concludes that the essential factor in curing warts by suggestion is the production of an inflammatory reaction by a psychic influence.

THE TREATMENT OF VARICOSE VEINS BY THE INJECTION OF GLYCERIN. MAX WOLF, Dermat. Wchnschr. **93**:1859 (Nov. 28) 1931.

The author injected a glycerin solution, consisting of 126 Gm. of glycerin and 200 cc. of water, into the varicose veins of 310 patients. In most instances, a satisfactory result was obtained.

AUTOVACCINATION PLUS VITAMIN FEEDING IN STAPHYLOCOCCIC INFECTION OF THE SKIN. MARTIN SCHUBERT, Dermat. Wchnschr. **93**:1864 (Nov. 28) 1931.

Experimentally produced staphylococcic infections of the skin of rabbits did not clear up any more rapidly than usual when the animals were fed a proprietary vitamin-calcium preparation. The combination of this treatment with vaccine was also useless. The combined treatment was not helpful in treating staphylococcic infection of the skin of human beings.

ICHTHYOSIFORM ERYTHRODERMA. S. LIEBERMANN, Dermat. Wchnschr. **93**: 1881 (Dec. 5) 1931.

The author reviews the literature in regard to this condition, pointing out the numerous titles that have been given to a group of conditions which probably belong in one category. He discusses the variations that have been reported. The patient, a woman, aged 33, had suffered from her cutaneous condition for thirty years. It consisted of a generalized, dry, red, exfoliative eruption with linear groups of grayish-white keratotic lesions on the neck, axillae, flexures of the elbows and popliteal spaces. There was an atrophy of the distal phalanges of the fingers and toes. The genitalia were infantile, and the patient had never menstruated. Roentgenologically, the joints showed a destructive chronic arthritis. There was no history of a similar condition in any other member of the family.

IMPETIGO HERPETIFORMIS IN A MAN WITH SEVERE INFECTIOUS POLYARTHRITIS AND CHANGES IN THE NAILS. EMANUEL WOHLSTEIN, Dermat. Wchnschr. **93**:1888 (Dec. 5) 1931.

A man, aged 31, had noted the gradual development of an arthritis, which after two years began to assume a deforming character. At about this time, a cutaneous condition appeared, first involving the axillae and genitocrural regions. He was seen after the disease had been present for four years. The eruption covered most of the body except the chest, shoulders and neck, but was most marked in the inguinal regions, axillae and lower part of the abdomen. The individual lesions were groups of clear vesicles around more or less crusted centers. Itching had previously occurred, but was not noteworthy at the time of examination. The general condition of the patient was poor.

CALCINOSIS ASSOCIATED WITH SCLERODERMA. ALFRED PERUTZ, Dermat. Wchnschr. **94**:189 (Feb. 6) 1932.

In a case of calcinosis associated with scleroderma, the lime function test of Hetényi showed a normal calcium curve. Parathyroid hormone caused only a slight increase in calcium in the blood. Scleroderma with calcinosis is not a disturbance of calcium metabolism, but is caused by a firmer fixation of the lime salts in the tissues.

A SEVERE HEMORRHAGIC DIATHESIS IN A 1½ YEAR OLD CHILD BENEFITED BY INTRAMUSCULAR INJECTIONS OF CALCIUM AND BLOOD. LADISLAUS GOLDSMITH, Dermat. Wchnschr. **94**:198 (Feb. 6) 1932.

In a 1½ year old boy severe purpura developed. The condition cleared rather rapidly under the influence of intramuscular injections of a calcium gluconate solution along with injections of the whole blood.

PSEUDOXANTHOMA ELASTICUM (DARIER) AND ANGIOID STREAKS OF THE RETINA IN TWO BROTHERS. WALTHER KRANTZ, Dermat. Wchnschr. **94**:233 (Feb. 13) 1932.

The author observed a 43 year old man who presented a typical pseudoxanthoma elasticum, confirmed by biopsy. The patient also presented angioid streaks

of the retina with areas of degeneration. One of his brothers presented the same combination of diseases though in lesser degree. Seven other cases of this association have been presented in the literature, and Krantz suggests that these two conditions may always occur together, pointing out that a number of the cases reported as pseudoxanthoma elasticum do not properly belong to this group.

THE CULTIVATION OF VACCINE VIRUS IN TISSUE CULTURE. E. G. NAUCK and E. PASCHEN, Dermat. Wchnschr. **94**:238 (Feb. 13) 1932.

The authors review briefly the previous work done in the cultivation of vaccine virus and describe their method of preparation of a tissue culture. They note a marked increase in virulence with succeeding passages and also a corresponding increase in the number of Paschen bodies.

HORMONAL DERMATOSES OF WOMEN: II. ACNE SEXUALIS. ROMAN v. LESZCZŃSKI and STANISLAW LIEBHART, Dermat. Wchnschr. **94**:261 (Feb. 20) 1932.

The authors divide acne into three main forms: (*a*) acne, sexualis, (*b*) acne intestinalis and (*c*) acne thyreogenes et seborrheica. They discuss the chief clinical features of these types and point out the indicated therapy based on the correction of the cause. External treatment is also advised in association with the specific therapy. Fifteen illustrative cases are reviewed briefly.

THE PATHOGENESIS OF EARLY DIFFUSE ALOPECIAS (ALOPECIA SEBORRHEICA, ALOPECIA PITYRODES). ARMAS CEDERBERG, Dermat. Wchnschr. **94**:272 (Feb. 20) 1932.

In studying 102 cases of early alopecia, the author found that 92 of the patients had mild seminal vesiculitis. He believes that this condition acts as a focus of infection in determining the development of the disease.

THE CONNECTION BETWEEN SYPHILIS, ARSPHENAMINE AND SO-CALLED CATARRHAL JAUNDICE ON THE BASIS OF 2,500 CASES OBSERVED IN THE NAVY BETWEEN 1919 AND 1929. HEINRICH RUGE, Dermat. Wchnschr. **94**: 278 (Feb. 20) 1932.

The author concludes as a result of his extensive observations that the jaundice occurring in the course of syphilis is due to the same agent (likely a member of the Bacillus coli typhoid group) as catarrhal jaundice. The somewhat higher incidence of jaundice in the syphilitic group was assumed to be due to a predisposing effect on the liver of the preceding syphilis and arsphenamine.

SEBORRHEIC ECZEMA OF UNNA OR SCHIZOSACCHAROMYCOSIS OF BENEDEK? IV. THE PRESENCE OF SCHIZOMYCETES IN THE BLOOD STREAM. W. ENGELHARDT, Dermat. Wchnschr. **94**:305 (Feb. 27) 1932.

In 115 cases, Engelhardt was unable to find schizomycetes in the blood stream either by culture or in smears of centrifugated blood. Benedek's method were rather closely followed. Various opportunities for error are discussed.

TELANGIECTASIA IN SYPHILIS. CARL SPEIERER, Dermat. Wchnschr. **94**:311 (Feb. 27) 1932.

In a 43 year old woman, progressive telangiectasia of the feet, legs and thighs, had developed, starting eighteen years before presentation. Four years previously she noted pain in the legs which gradually became worse. The Wassermann test

of the blood was positive. Antisyphilitic therapy caused cessation of the pains, and no further telangiectases appeared. Syphilis should always be considered as a possible cause of otherwise unexplained telangiectasia.

TAUSSIG, San Francisco.

POLYNEURITIS FOLLOWING NEOARSPHENAMINE THERAPY OF SYPHILITIC ICTERUS. A. OLIVET, Deutsche Ztschr. f. Nervenh. **123**:288 (Jan. 21) 1932.

Olivet gives the clinical histories of two syphilitic patients, who, following the development of the primary lesion, underwent treatment with neoarsphenamine and mercury or with bismuth. Five months later a hepatic relapse with icterus developed and the Wassermann reaction was weakly positive. A second neoarsphenamine-bismuth treatment was instituted, and as a result the icterus disappeared and the Wassermann reaction became negative. Toward the end of the second treatment, from six to seven months after the primary lesion, prolonged polyneuritis developed; the Wassermann reaction in the blood remained negative but in the cerebrospinal fluid it was found positive. In the beginning the polyneuritis was progressive; later there was a slow but almost complete recovery. Syphilitic symptoms did not recur. In discussing the pathogenesis of the polyneuritis, the author reaches the conclusion that the decisive factor was that the neoarsphenamine treatment was carried out during an impairment of the renal parenchyma. The liver was not able to decompose and to detoxicate the substance, and thus the neoarsphenamine exerted a toxic neurotropic action. On the basis of these experiences the author advises caution in the treatment of syphilitic icterus with neoarsphenamine. To avoid similar injuries he recommends the trial of small doses of neoarsphenamine and a close watch for the first signs of polyneuritis, such as pains, paresthesias, disturbances in sensibility and weakening of the tendon reflexes.

EDITOR'S ABSTRACT. [J. A. M. A.]

COMPARATIVE STUDIES OF STOMATITIS CAUSED BY DRUGS FROM THE GROUP OF HEAVY METALS. A. HEINDL, Monatschr. f. Ohrenh. **65**:1467 (Dec.) 1931.

Heindl describes and compares several cases of stomatitis resulting from therapy with mercury, bismuth and gold preparations and briefly reviews some of the literature pertaining to this subject. The author thinks that intoxication with one of these metals is not the specific cause of the stomatitis which often follows but is to be considered as a predisposing influence which, together with a possible syphilitic infection, prepares the ground for bacterial infection. Intoxication with a preparation of one of these metals, besides producing a lowering of vitality, disturbs the nutrition of the tissues and decreases the bactericidal action of the saliva, thereby favoring the invasion of the tissues by the bacteria present in the mouth. A harmless inflammatory process of the gums and mucous membrane is thus transformed into a serious necrotic process. If the tissues have been weakened by syphilitic infiltrations, the development of a stomatitis is favored. The presence of decayed teeth and the use of tobacco and fresh fruit are considered contributing factors in the development of stomatitis. The author suggests that therapy with any preparation of the heavy metals be preceded by a thorough examination of the teeth and possible extraction of diseased teeth. During and after therapy, the mouth should be cleansed several times daily with hydrogen dioxide because of its prompt effect in combating the anaerobic bacteria chiefly concerned in this infection. The use of tobacco and eating of fresh fruits are to be avoided during the course of treatment, and the close observation of kidney function and the corresponding regulation of diet are advised.

EDITOR'S ABSTRACT. [ARCH. OTOLARYNG.]

THE FATE OF CEREBROSPINAL SYPHILIS CASES TREATED WITH MALARIA. FRANZ GUGENHEIM, Ztschr. f. d. ges. Neurol. u. Psychiat. **131**:525 (Jan.) 1931.

There have been very few studies of malaria-treated cerebrospinal syphilis, in contrast to the many studies of this treatment in paresis. Gugenheim reports thirteen or fourteen cases, or 93 per cent of cerebrospinal syphilis in which the spinal fluid was cleared up by a combination of malaria and arsphenamine. This clearing of the fluid is not dependent on the severity of the spinal fluid changes. The Wassermann reaction of the blood was rendered negative in twelve of eighteen cases, or in 66.7 per cent. There is a close relationship between the clearing up of the fluid and the success of treatment.

Of the fourteen cases reported, 60 per cent of the patients were rendered free from complaints and able to work, 12 per cent were markedly improved, 16 per cent were improved, 8 per cent were unimproved, and 4 per cent were rendered worse.

Behring's studies of the effect of malaria on cerebrospinal syphilis show: (1) that there is little danger to life; (2) that all cases with positive spinal fluid tests show improvement under the treatment; (3) that clearing up of the spinal fluid goes hand in hand with clinical improvements; (4) that the more recent the infection of the nervous system, the better are the results.

ALPERS, Philadelphia. [ARCH. NEUROL. & PSYCHIAT.]

HISTOLOGIC REGRESSION OF EPITHELIOMAS OF THE LYMPH GLANDS FOLLOWING ROENTGEN THERAPY. A. TOBECK, Ztschr. f. Hals-, Nasen- u. Ohrenh. **30**:182 (Dec. 18) 1931.

Tobeck contributes a discussion of the question as to whether epitheliomas of the lymph glands may justly be classified in a separate group, or whether they are to be considered as carcinomas with secondary lymphocytic infiltration. He gives a negative answer based on the histologic effect of roentgen treatment of a tumor of the palatine tonsil diagnosed as an epithelioma of the lymph glands. Three treatments were given, and biopsies were made before roentgenization, between treatments and at intervals for one month thereafter. Roentgenization was followed macroscopically by a rapid disappearance of the tumor. Microscopically, it was followed by a rapid disintegration of the epithelial components of the tumor accompanied by a relatively good preservation of the lymphocytic components. The rapidly developing granulation tissue was at first rich in plasma cells and later, during cicatrization, in mast cells. In view of the histologic effect of roentgenization on the rapid disintegration of the epithelial components, preservation of the lymphocytic components and the rich development of cells removable by lymphocytes, the author considers the separate classification of epitheliomas of the lymph glands of doubtful justification. He thinks that epitheliomas of the lymph glands are rather to be considered as carcinomas composed of young, slightly differentiated and therefore roentgen-sensitive epithelial cells with secondary infiltration of lymphocytes.

EDITOR'S ABSTRACT. [ARCH. OTOLARYNG.]

THE CULTIVATION OF SPIROCHAETA PALLIDA. R. R. HÖLTZER, Ztschr. f. Immunitätsforsch. u. exper. Therap. **72**:320, 1931.

The so-called "cotton" culture mediums of Wrublewski, consisting in the use of cotton instead of animal tissues for adsorption of oxygen, proved unsatisfactory for growing Spirochaeta pillada. However, addition of 10 per cent rabbit or sheep serum gave a luxuriant growth, equal to the one obtained in broth containing pieces of liver. A layer of petrolatum on the surface to exclude oxygen was necessary for the growth.

I. DAVIDSOHN. [ARCH. PATH.]

# Society Transactions

## NEW YORK ACADEMY OF MEDICINE, SECTION OF DERMATOLOGY AND SYPHILIS

LEO SPIEGEL, M.D., *Secretary*

*Jan. 5, 1932*

JOSEPH J. ELLER, M.D., *Chairman, Presiding*

DERMATOPHYTOSIS AND DERMATOPHYTID (OIDIOMYCOTICA?). Presented by DR. MARION B. SULZBERGER.

S. Y., a woman, aged 43, married, was first seen at the skin clinic of the New York Post-Graduate Hospital on May 6, 1930, with an eruption of three months' duration. On examination an erythematous lesion was found on the dorsum of the left hand and index finger. Microscopic examination for fungi yielded negative results.

The patient responded well to local treatment and suffered no recurrence until April 9, 1931. She then showed evidence of severe dermatophytosis between the toes and quarter-sized patches of vesicles on the dorsum of both hands, the right thigh and the left arm.

Skin tests yielded the following results: (1) oidiomycin (intradermal) — + +; (2) oidiomycin (patch test) — —; (3) trichophytin (diluted 1:30) + +; (4) trichophytin (patch test with 1:10 solution in affected areas) + +; (5) trichophytin (patch test with 1:10 solution in unaffected areas) —.

Desensitization was begun on Dec. 25, 1931 with oidiomycin and trichophytin. In forty-eight hours the reaction to the intradermal injections appeared as an area of erythema and induration one-half inch (1.2 cm.) in diameter. One week after injection the locus of reaction showed central clearing surrounded by a zone of vesicles, pin-point in size, and annular configuration with superficial scaling, in other words, an eczematous eruption of the same type as the original lesions.

The desensitization with oidiomycin and trichophytin was being continued at the time of presentation.

### DISCUSSION

DR. MARION B. SULZBERGER: I presented this case not because the clinical lesions are unusual, nor because not enough has been said about this condition, but because of some special features that merit attention. A clinical diagnosis was made of dermatophytosis of the feet and dermatophytid of the hands. The patient was tested with trichophytin and found to react positively. She also gave a positive reaction to a patch test with trichophytin, not on normal skin, but on skin previously affected by lesions. I think that an interesting feature. In this case one must apply the test near to or on the healed area to get a reaction of hypersensitiveness. If one considers the pathogenesis of these lesions, one realizes that this must be so in some cases. If the fungous products are being disseminated throughout the blood stream, the reaction of the skin must take place in the areas in which this sensitiveness resides. This patient reacts not only to trichophytin but also to oidiomycin in a manner in which normal controls do not. I think that there are mixed infections among the dermatophytids. I have seen patients who reacted to each extract (trichophytin and oidiomycin) individually, and some who reacted to both.

Our percentage of cures is better since I have been considering both of these types of fungi (Trichophyton and Monilia) as unrelated to each other immunologically and attempted to desensitize the patient to both.

These cases show scaling, eczematous patches at the sites of injection, exactly simulating the lesions on the hands. The resemblance in this particular instance was even greater when one observed that the patches spread peripherally and became annular, showing all the elements of parasitic skin lesions, owing to the invading organism attacking new areas of skin. J. Jadassohn has repeatedly pointed out that this reaction also occurred to nonliving substances, and that it was an immunologic desensitization phenomenon.

DR. FRANK C. COMBES, JR.: The negative patch test on the normal skin in this case is of particular interest. Is it possible to test patients with trichophytin by means of passive transfer? I have never heard of this being successfully performed.

DR. MARION B. SULZBERGER: In answer to the question, this is an eczematous type of eruption. In this type of eruption, I have not found it possible to transfer the sensitiveness with the blood. However, the experiments of Dr. Kerr and myself showed that in a case showing an urticarial, immediate reaction to trichophytin, we could transfer this type of sensitiveness (immediate wheal) to a normal person (Sulzberger and Kerr: Trichophytin Hypersensitiveness of Urticarial Type with Circulating Antibodies and Passive Transference, *J. Allergy* **2**:11 [Nov.] 1930).

PEMPHIGUS (?). DERMATITIS MEDICAMENTOSA (?). Presented by DR. ISIDORE ROSEN.

Y. T., a woman, aged 31, born in Russia, called at the clinic on Jan. 4, 1932. She stated that one year previously she was burned on the abdomen with some hot water, and since that time the eruption had been present.

Examination revealed on the abdomen, in the region of the umbilicus, three irregularly outlined patches composed of crusted and bullous lesions. There was one pea-sized bullous lesion arising from the normal skin. Just above the umbilicus there was a *café-au-lait* spot the size of a dollar. There were lesions within this spot. Over the lumbar region there were two or three coin-sized patches composed of dry crusted lesions. There were two petechial lesions on the right buccal mucous membrane.

DISCUSSION

DR. HARRY ALDERSON: Is there any possibility that these lesions were self-inflicted? They are symmetrical and have an artificial appearance. The eruption is unlike anything else.

D. ABRAHAM WALZER: The patient was under our care for about two months at the Good Samaritan Dispensary. She first had an erythematous spot around the umbilicus which she attributed to a burn. Under mild applications she improved, but she returned after a short time with bullous lesions on that spot, which were gradually extending. While under our care she took practically no drugs. She denied taking any drugs previous to that time. We labeled the condition "a bullous eruption of some unknown origin."

DR. SIGMUND POLLITZER: Did this woman really have a burn?

DR. ABRAHAM WALZER: We did not see the burn. She told us that she had had it.

DR. SIGMUND POLLITZER: It seems possible that this case could be grouped in the class called contagious pemphigus, in which bullae follow a trauma and continue appearing for a long time, somewhat analogous to an acute pemphigus.

LICHEN PLANUS. Presented by DR. HERMAN GOODMAN.

A. B., aged 26, white, single, came to the Stuyvesant Square Hospital clinic on Dec. 8, 1931, because of pink to violaceous, shiny papules in a linear distribu-

tion, situated on the left shoulder and outer aspect of the left arm. There were several papules on the inner aspect of the left forearm. These lesions were accompanied by itching at their onset, two and a half months before the patient's admission to the clinic.

There was also slight swelling of the right arm, and the superficial veins of the right shoulder and chest were dilated and prominent.

The past history was irrelevant except for marked nervousness, especially during the previous three months.

The Wassermann reaction was negative. At biopsy, no diagnosis was made. The epidermis was rather irregular. There was marked edema in places, just below the basal cell layer. Examination was negative for lichen planus. A second biopsy was done which showed no evidence of lichen planus.

DISCUSSION

DR. HERMAN GOODMAN: I made the clinical diagnosis of lichen planus linearis on the basis of the linear arrangement of the papules along the upper arm, and the circlet of papules close to the neck. Histologic examination of two pieces of skin removed at different times did not sustain this diagnosis. The patient had treated herself for some time with radiation from an ultraviolet source. I am of the opinion that this has altered the familiar microscopic picture of lichen planus — that of the subsiding rather than the immediate phase. If this condition is not lichen planus, I have no substitute clinical diagnosis to offer.

The enlarged veins of the right side of the neck and upper part of the chest have been noted, and a cursory clinical examination has not disclosed any pathologic condition of the chest. A roentgenogram will be taken and reported later. (The roentgenologist reported no pathologic indications in the chest or mediastinum.)

DR. DAVID BLOOM: There are no shiny, violaceous papules present. I believe, therefore, that this is a case of linear dermatitis or eczema which one sees occasionally and which disappears after a short time. The prominent veins on the right upper part of the chest and the marked enlargement of the upper part of the right arm in contrast to the left speak for an obstruction and may possibly be the cause of the linear eruption on the left side.

DR. SIGMUND POLLITZER: Obviously the patient has a subclavian tumor, causing an obstruction to the return flow.

MYCOSIS FUNGOIDES. Presented by DR. MORRIS LYONS.

S. E., a man, aged 78, was admitted to the skin clinic of the New York Post-Graduate Hospital on Sept. 1, 1931. Over the trunk and extremities, especially the lower extremities, were many large, irregularly shaped areas. These were slightly elevated, sharply marginated and infiltrated. In places they formed large plaques and patches. Posteriorly, on the right inner aspect of the right thigh, there was a large mass the size of a hen's egg. The patient complained of considerable pruritus. The color of the eruption was a dull pink.

Since admission the patient had received roentgenotherapy with improvement.

Biopsy confirmed the clinical diagnosis of mycosis fungoides.

DISCUSSION

DR. E. WILLIAM ABRAMOWITZ: I treated this patient about ten years ago. The diagnosis of mycosis fungoides was at that time confirmed by biopsy. Previous to this the patient had been under the care of Dr. George Henry Fox, who also made a microscopic examination of a piece of skin from one of the lesions, and confirmed the diagnosis of mycosis fungoides. The duration of this condition, judging from the history given to me at that time, is now close to thirty years.

ECCHYMOSIS AND PURPURA, FOLLOWING BISMUTH (?). Presented by DR. E. WILLIAM ABRAMOWITZ.

M. K., a woman, aged 31, born in Austria, came to the clinic of the New York Post-Graduate Hospital for treatment of a varicose ulcer on the lower third of the left leg. As she did not respond to treatment with the usual local remedies, she received three injections of bismuth salicylate. The last injection was given on Oct. 28, 1931, and a week later she reported at the clinic with the complaint of an eruption on the body. Since then there had been recurrent hemorrhagic patches on the trunks and extremities, with a purpuric eruption on the legs. Patches on the back appeared two days prior to presentation. She denied taking any laxatives, headache powders or other drugs.

DISCUSSION

DR. HERMAN FEIT: I think that this kind of eruption is of the greatest importance, although bismuth as an etiologic factor is doubtful. It may be that the bismuth preparation is contaminated with arsenic. The same thing that happened to the skin, namely, the purpura, can occur in the meninges of these patients who are sensitized to metals. So-called encephalitis hemorrhagica is nothing but a purpura cerebri, as I had occasion to convince myself at an autopsy in Berlin many years ago. Purpuric cutaneous lesions following injections of silver arsphenamine were first described by me, and the possibility of hemorrhages in the brain of such sensitized patients points out this fact.

DR. OSCAR LEVIN: I prefer looking on this case as indicating not that there is sensitization to bismuth but that the bismuth has had a toxic effect on the walls of the blood vessels and resulted in the hemorrhage into the skin. Patients of this type should have general examinations, especially as regards the functions of the kidneys and the liver, as these organs may also be involved in the damage produced by the drug.

DR. E. WILLIAM ABRAMOWITZ: More than a half dozen cases of purpura following injections of bismuth have been reported in the foreign literature. Such reactions are probably due to the toxic action of the metal on the walls of the vessels. As soon as an opportunity presents itself, we will attempt to prove whether or not the ecchymotic and purpuric spots recur on further injections of bismuth. The patient's skin will also be treated for hypersensitiveness. A complete blood count has been ordered.

LUPUS ERYTHEMATOSUS OF THE FACE (IN BROTHER AND SISTER) TREATED WITH COLLOIDAL BISMUTH OINTMENT. Presented by DR. E. WILLIAM ABRAMOWITZ.

D. B., a girl, aged 18, born in the United States, had always been in perfect health until two years prior to presentation, when a penny-sized, sharply defined, raised, red scaly lesion appeared in the center of the left cheek. There was a pea-sized similar lesion above it which had appeared recently. There was no history of sunburn or other injury. Biopsy confirmed the diagnosis of lupus erythematosus.

U. B., a brother of this girl, aged 35, born in the United States, had been shown before the section about one year prior to this presentation, with erythematous and atrophic patches of bat-wing distribution, and patches of lupus erythematosus following a severe sunburn and the application of vinegar. Biopsy confirmed the diagnosis of lupus erythematosus.

The sister had been under treatment with bismuth ointment, applied locally, only since October and had shown marked improvement. The brother had been receiving injections of a gold preparation, but his eruption had become aggravated. It was decided, after the fourth injection, to stop this treatment and give him bismuth intramuscularly and bismuth ointment locally. He had been under that therapy for the past five months and had shown rapid improvement. The formula for the ointment was that advocated by R. M. B. MacKenna of Liverpool.

DISCUSSION

DR. MARION B. SULZBERGER: Where can one obtain MacKenna's bismuth oxychloride ointment?

DR. E. WILLIAM ABRAMOWITZ: I should like to call the attention of the members to the fact that I am presenting a brother and sister both of whom have lupus erythematosus of the face. This is an unusual occurrence. The brother received five injections of gold and sodium thiosulphate, but as the lesions on the face became distinctly worse, he was put on weekly intramuscular injections of bismuth, and applications of a bismuth ointment to the lesions on the face. The sister received only the ointment. A decided improvement was noted in both, following the use of this metal preparation.

R. M. B. MacKenna, of Liverpool, in the *Lancet* (**1**:126 [Jan. 17] 1931), first advocated the local use of bismuth ointment in cases of lupus erythematosus. It is a colloidal bismuth oxychloride made by the St. Vincent Laboratories in Glasgow. The laboratory was kind enough to send me some samples for trial. Through the kindness of Dr. Rosen's brother, who made an additional supply of the ointment, we have been able to treat a few other patients suffering from this disease, with rather encouraging results.

ACRODERMATITIS CHRONICA ATROPHICANS. Presented by DR. J. L. MORSE.

D. P., a woman aged 58, from the clinic of the New York Post-Graduate Hospital, had had the present eruption for six years; it was located on the dorsal aspect of the right hand and forearm. The skin was puffy, almost boggy in appearance, and violaceous, with marked wrinkling and an increase in the skin markings. The patient had been previously presented before the New York Dermatological Society by Dr. Wise. There was a pea-sized fibrous nodule over the metacarpophalangeal joint of the little finger; a smaller nodule was located over the index finger. There was a boggy infiltration on the ulnar side of the forearm near the elbow, which was violaceous and shiny. Just below the elbow was a walnut-sized subcutaneous nodule, which was freely movable. There was a slightly boggy area on the dorsal aspect of the left hand. The lower extremities were free from lesions. The Wassermann reaction was negative. The basal metabolic rate was three plus. Biopsies were taken from the nodule on the back of the right hand and right elbow, and the pathologic pictures corresponded to acrodermatitis chronica atrophicans (nodular type).

DISCUSSION

DR. OSCAR LEVIN: On the right forearm and elbow the patient presents a diffuse, purplish, dark red condition associated with numerous telangiectasias and tumor-like formations, especially over the bones and elbow. The infiltrations are very hard and attached to the deeper structures, and suggest the lesions of a fibroid syphiloma. The complete condition is probably due to syphilis. Acrodermatitis chronica atrophicans is suggested, only to be ruled out.

DR. MARION B. SULZBERGER: The patient shows diffuse atrophy of one arm and juxta-articular nodosities. These nodules are also seen in syphilis and in frambesia. There has been a great deal of discussion as to which type of spirocheticidal infection causes this type of nodule. This case *with its nodules* (frequently described by many observers) is a typical acrodermatitis, clinically, with the exception of its unilateral localization. Of course syphilis has been ruled out by serologic examination and other procedures.

DR. HERMANN FEIT: Herxheimer, who described this disease, pointed out that these nodules occur mostly on the ulnar side, just as in the case presented here. Syphilis can be ruled out on account of the long duration (from five to six years) without change, although hypodermic syphilomas do not show much alteration.

DR. FRANK C. COMBES, JR.: I agree with the diagnosis of acrodermatitis chronica atrophicans. I consider the lesions at the elbow to be juxta-articular

nodules, frequently seen in this condition. On close examination I thought that I would detect in addition an ulnar band of scleroderma.

DR. HERMAN GOODMAN: On clinical inspection, the lesions presented by this patient led me to believe that she had a subcutaneous nonulcerative syphiloma. The distribution (unilateral) is unusual. All the cases that I have seen have been bilateral and unusually symmetrical. The serology, microscopy and effect of antisyphilitic therapy should clarify the diagnosis.

Subsequent biopsy revealed the usual fibrotic histologic changes described in acrodermatitis chronica atrophicans.

ULCERATION OF THE WRIST. Presented by DR. JOSEPH J. ELLER.

This patient was previously presented before the section at the November, 1931, meeting. Additional biopsies were taken from a new lesion and from the edge of the large ulceration of the wrist. On microscopic examination the former was suggestive of mycosis fungoides. At present, the patient has a number of large nodules on the face covered with heavy rupial crusts, strongly simulating a case of fatal ioderma. Urinalyses have given negative results for iodides and bromides.

DISCUSSION

DR. LOUIS CHARGIN: I did not discuss the case when it was presented before the section. I was uncertain as to the diagnosis. However, I had no hesitation in making a diagnosis of mycosis fungoides from a mere glance at the patient when he was presented before another society about two weeks later. At the last presentation, the patient presented tumor-like infiltrations at the sites of the former macular lesions. These were bluish red and of elastic consistency. Some were superficially ulcerated and one could hardly doubt that a mycosis fungoides d'emblée was present.

DR. J. FRANK FRASER: The two sections were given me by the chairman for microscopic study. One was taken from the primary lesion, the other from a new lesion. The whole difficulty starts with the problem of what mycosis fungoides really is. The histologic picture here is exactly the same as that usually found in the clinical syndrome that is recognized as mycosis fungoides. I feel, therefore, that we are justified in saying that the microscopic observations support the clinical diagnosis of mycosis fungoides. The nature of the cells in the histologic picture of mycosis fungoides was recently described by Pollitzer (Pollitzer, S., in discussion of Ketron, L. W., and Goodman, M. H.: Multiple Lesions of the Skin, Apparently of Epithelial Origin Resembling Clinically Mycosis Fungoides, ARCH. DERMAT. & SYPH. **24**:779 [Nov.] 1931).

MIKULICZ' SYNDROME IN A CASE OF LYMPHOBLASTOMA WITH CUTANEOUS MANIFESTATIONS. Presented by DR. HERMAN FEIT.

This patient was presented before the Section at the previous meeting. A biopsy showed infiltration of the corium consisting of round cells, presumably lymphocytes. There were also polymorphonuclears and eosinophils. There was large massive infiltration of lymphocytes and large mononuclear epithelioid cells. In these areas was some evidence of necrosis and polymorphonuclear infiltration.

ERYTHRODERMA FROM BISMUTH. Presented by DR. E. WILLIAM ABRAMOWITZ.

This patient was presented before the section at the previous meeting.

DISCUSSION

DR. ABRAHAM WALZER: How were the tests done?

DR. E. WILLIAM ABRAMOWITZ: Patch tests were done.

DR. ABRAHAM WALZER: The skin of a patient having a generalized erythroderma is not suitable for such tests. The fact that the patients show reactions on a diseased skin site does not presuppose a sensitivity to that substance. A normal site must be employed.

DR. J. GARDNER HOPKINS: It would seem to me difficult to test a patient with a generalized erythroderma for sensitivity. What type of reaction did Dr. Sulzberger find? I should also like to ask whether he has found the patch test with arsphenamine satisfactory in an exfoliative or eczematous type of dermatitis. In the intracutaneous tests the reaction is hard to read.

DR. MARION B. SULZBERGER: The type of reaction to the patch test was of an eczematous character: papular, vesicular, erythematous and eventually scaly, both with a solution of potassium arsenite and with arsphenamine. The solutions employed were both tested on controls and caused no reaction.

Regarding Dr. Hopkins' second question, I would say yes and no. I think that as a test to determine whether a patient is likely to get an arsphenamine dermatitis the patch method, as used by Chargin and myself, has not been of value. A positive patch test does not necessarily mean that the patient has had arsenic medication before. The ways in which arsenic enters the system are so manifold that we cannot exclude these multitudinous possibilities. Lastly, Dr. Stokes, in using the patch test in arsphenamine dermatitis, tells me that he finds, if the patient has had arsphenamine dermatitis and is tested by means of the patch test some time afterward and does not react with an eczematous patch, that it is relatively safe to give arsphenamine again, whereas, if there is a strong reaction, arsphenamine will probably cause a dermatitis. I myself have never used the patch test in this way.

DR. OSCAR LEVIN: It seems to me that we confuse the relationship of the chemicals to the cutaneous condition in this case. Although the patient has a bismuth dermatitis and the skin showed a reaction to the drug on local application, it seems to me that this does not prove the specificity of the reaction. The skin was so inflamed that any irritant or chemical might have produced the same local reaction. We should differentiate between sensitivity and susceptibility to the chemicals. Sensitivity is acquired, while susceptibility is a congenital or acquired subnormal condition in which the skin is more easily affected by irritants. The reaction that the patient shows depends on the mass, strength, concentration and length of exposure to the irritant. In sensitization, the skin may be perfectly normal to ordinary irritants, but may have a physicochemic affinity for, or antagonism to, specific agents. The reaction depends entirely on the degree of sensitization. A small amount of the irritant may produce an unexpected and profound response.

DR. SAMUEL PECK: It has been my idea that it is dangerous to use arsphenamine intradermally as a method of testing for hypersensitivity. The work of Nathan and Monk as well as Frey has shown that many of the patients given intradermal injections of small amounts of arsphenamine eventually became hypersensitive to it.

DR. HERMAN FEIT: When I saw this patient at the last meeting, I suggested arsenic as the cause, because many bismuth preparations are supposed to contain this metal, according to Dr. C. N. Myers. The patch test seems to bear out this assumption. I would suggest an investigation of this matter so that we may really know what we are giving to the patients.

DR. J. GARDNER HOPKINS: I do not think that the statements of Dr. Peck should pass without comment. The first work on tests for arsphenamine sensitization was done at the Presbyterian Hospital by Stuart and Maynard over ten years ago. Many patients were tested intradermally, and there has been no evidence that any of them were sensitized by this procedure. Since then Dr. Cannon and Dr. Karolitz have performed many such tests, and I do not believe that in any case they have sensitized the patient.

DR. A. BENSON CANNON: It is interesting that this patient should react to tests with arsenic. I am informed by Dr. Myers that the great majority of bismuth preparations contain large amounts of arsenic, often from 11 to 15 per cent, as a by-product in the manufacture of the compound. In view of the positive skin tests to arsenic in this instance, I should think it highly probable that the condition is arsenical dermatitis rather than due to bismuth. We have performed a great many skin sensitization tests with arsenicals in the past few years, and we have never seen a sensitization develop from intracutaneous skin tests that has prevented intravenous injections of the arsphenamines. I think, as does Dr. Hopkins, that such an instance must be exceedingly rare. It is true that an arsphenamine dermatitis will often develop following an infiltration of the drug in the tissue at the site of injection, but I doubt the possibility of skin tests producing the same condition unless they are repeated at frequent intervals over a considerable period of time.

DR. HERMAN GOODMAN: If all bismuth preparations contain arsenic, and the patient is sensitive to arsenic, why does he not react to the arsenic quotient of the bismuth? Some other factor must be uncovered. Were the test products equally soluble, for example?

DR. SAMUEL PECK: The work of Sulzberger as well as some American reports have shown that it is possible to produce hypersensitivity by very small amounts of arsphenamine injected intradermally. Ebert has reported peculiar changes in the skin following intradermal injections of arsphenamine which resembled epitheliomas.

DR. MARION B. SULZBERGER: I think that the first work on experimental arsphenamine sensitization was done by Frei in Breslau. I believe that his statistics were that he sensitized eight of sixty-six patients with 0.1 cc. of a solution of arsphenamine, 0.15 Gm. in 100 cc. These eight became sensitized in such a manner that they gave marked inflammatory reactions to the arsphenamine solution on subsequent intradermal injection. Of course this does not mean that these patients must get dermatitis from subsequent intravenous injection, but in the light of our present knowledge, it would seem to make this more likely. For this reason we abandoned this method as being too hazardous, and I have never since given an intradermal injection of arsphenamine.

DR. J. GARDNER HOPKINS: I think that there may be a difference in type or degree between the sensitization produced experimentally in guinea-pigs and that which causes the dermatitis in human beings. The fact that guinea-pigs that have received intradermal injections later give a positive reaction does not prove that patients who have been given intradermal injections are in any danger of developing dermatitis from subsequent injections. Long experience with these tests practically rules out this possibility.

DR. ABRAHAM WALZER: To admit a sensitivity because a reaction of some sort was obtained on a diseased site of skin is, I think, going a little too far. The fact that control tests were made on the skin of different persons has no bearing on this case. The capillaries of diseased skin may react nonspecifically to many substances, especially when they are in an actively inflamed state, or they may not react at all, owing to a temporary refractoriness. This patient, therefore, should not go on record as being sensitive to arsenic purely on the basis of such poor and unreliable testing.

DR. CHARLES WOLF: When this case was presented last month, I suggested a diagnosis of pityriasis rubra of Hebra. I still feel that this disease should be considered. It is strange that though bismuth was administered, a positive arsenical reaction was obtained. Arsenic has not been given to the patient. Pityriasis rubra of Hebra is associated with tuberculosis and may take a chronic course. Roentgenologic examination of the chest should be made.

DR. E. WILLIAM ABRAMOWITZ: When this patient was presented at the last meeting with an exfoliative dermatitis, following the intramuscular injections of bismuth subsalicylate, we called attention to the fact that, aside from the lupus

erythematosus of the face, he had had no previous eruption on the rest of the body. He gave no history of taking any medication; he had merely used some bland ointment on the lesions on his face. In view of the fact that a generalized eruption appeared for the first time following the use of bismuth, it was logical to blame this drug for the dermatitis.

Owing to the common and general use of the modern arsenicals, it is only natural, when one sees a case of exfoliative dermatitis, to think of arsenic as the cause. A few of the members therefore suggested arsenic as the cause in this case. It is known, however, that preparations of other metals, e. g., mercury, gold and bismuth, may also produce a similar dermatosis. In fact, the foreign literature cites numerous cases of exfoliative dermatitis (erythroderma) that followed the use of bismuth.

Soon after the patient's eruption faded somewhat on the back, we decided to carry out a number of patch tests using bismuth subsalicylate in a peanut oil and hydrous wool fat vehicle, then peanut oil and hydrous wool fat separately with other substances as a control. These were: a 1 per cent solution of neoarsphenamine, solution of potassium arsenite, 10 per cent bismuth oxychloride ointment, a 1 per cent solution of salicylic acid, and 1:1,000 corrosive mercuric chloride. A reading made twenty-four hours later showed a four plus reaction with the solution of potassium arsenite and a two plus reaction with the neoarsphenamine. The patient gave a negative reaction to all the other substances.

A second series of tests repeated a few days later gave similar results. All the substances mentioned had previously given negative results in normal persons. To my mind this shows that the patient's skin is susceptible to arsenic. Whether or not his exfoliative dermatitis is due to arsenic will require further observation.

I think that we can eliminate the possibility that the bismuth preparation used was contaminated with arsenic because if it had been, we should have had a reaction when we tested with the bismuth compound. (Dr. George W. Raiziss, in answer to my query as to arsenic contained in some of the bismuth preparations put out by the Dermatological Research Laboratories, said that bismo-cymol and potassium bismuth tartrate contained no arsenic on analysis. Bismuth salicylate showed a slight trace 1 mg. in 2 Gm.) The patient had plenty of opportunities of becoming sensitized to arsenic, because he had been a painter and also drank quite a lot of beer. It has been shown by Fordyce, Rosen and Myers that this metal is found not only in various foods but also in such applications as calamine lotion.

I do not think that the tests have in any way been rendered valueless, as Dr. Walzer seems to think, because they were done on skin that was not entirely normal. If anything, the positive reactions are of still greater importance, as it is known that areas of skin that have previously been affected through the use of a certain drug will often react with more vigor against that particular drug when it is used again. This is seen in the case of fixed drug eruptions after internal administration, and is also to be noted after the use of various medicated plasters.

The interesting point is raised — and this has been mentioned by other investigators — as to the possibility of one drug inducing a reaction after the patient harbors in his system some other chemical or biologic agent. Milian applies the term "biotrophism" to many of the untoward effects of drugs that he believes are due to a stimulation of a latent parasitic infection.

It is possible that the skin tests point to a sensitization to arsenic because of an arsenical retention in the tissues from exposure to this metal in some unknown way. The bismuth either activated this latent arsenical retention and caused the eruption to appear, or stirred up some quiescent infection that the patient harbored. As dermatitis exfoliativa following the use of a drug is usually considered as due to the direct toxic action of the drug, I am inclined to believe that the eruption is due to the bismuth activating a latent arsenical retention.

I see no evidence of the suggestion made by Dr. Wolf of a pityriasis rubra of Hebra. These cases are extremely rare, and the diagnosis is usually not made

until the patient is in extremis. We will examine him for evidences of tuberculosis. The patches of lupus erythematosus of the face have entirely disappeared, since the development of the exfoliative dermatitis. A biopsy will be ordered to study the skin histologically. (This was later reported by Dr. Satenstein as showing a low grade exudative inflammatory reaction. A twenty-four hour specimen of urine was examined for the presence of arsenic, and although the patient had been receiving calcium thiosulphate, the laboratory reported that no arsenic was found.)

ERYTHRODERMITE CONGÉNITALE ICHTHYOSIFORME. Presented by DR. LOUIS CHARGIN.

E. E., a saleswoman, aged 21, single, stated that her father had had "bad" nails. There were six children in the family, the patient being the youngest. No one in the family seemed to be affected except the eldest brother, whose feet and hands were unusually dry and scaly.

Inquiry revealed that the patient had always had redness of the skin even as an infant; there had also been considerable scaling, which required frequent rubbing with olive oil. The redness and scaliness had persisted and was most marked on the face, the outer surfaces of the arms and the upper part of the chest and over the extensors of the legs. The scalp was moderately affected, and was red, dry and more scaly than normal. The palms and soles were dry, scaly and fissured.

The disease of the nails was marked. Nearly all the finger nails were affected on both hands. They were deformed, narrow, fissured, shortened, hyperkeratotic and uneven on the surface. To some extent they resembled well advanced psoriatic nails. The toe nails were also affected, particularly the big toe nails.

The mucous membranes were not involved. It was to be noted that the flexors of the extremities were not affected.

DISCUSSION

DR. LOUIS CHARGIN: The erythroderma on the face, back, chest and outer surfaces of the arms and legs, the scaling on the outer surfaces of the arms and legs, the deformed nails and the keratosis of the palms and soles, together with the history of onset at birth, leave no doubt in my mind as to the diagnosis of erythrodermie congénitale ichthyosiforme. The fact that a brother suffers from a marked keratosis of the palms and soles further serves to confirm the diagnosis.

DR. OSCAR LEVIN: Will Dr. Chargin report on the basal metabolism determination and the appearance of the sella turcica at the next meeting?

DR. ISIDORE ROSEN: I do not agree with the diagnosis presented. While there may be mild types of erythrodermie congénitale ichthyosiforme, I fail to note any of the essential features present to warrant that diagnosis. This patient presents a xerotic skin with a vasomotor disturbance. There is no evidence of ichthyosis or erythrodermia, usually pronounced in erythrodermie ichthyosiforme. The palmar lesions are suggestive of psoriasis or a mycotic infection.

PSEUDOPELADE. Presented by DR. VAN ALSTYNE CORNELL.

J. P., a man, aged 23, born in the United States, had been presented at the last meeting of the Academy. There was some doubt about the diagnosis. A biopsy was taken, which revealed a mild form of perifolliculitis, not evident clinically. The scalp showed the "gulf and promontory" appearance that is rather characteristic of this disease. The Wassermann reaction was negative.

DISCUSSION

DR. E. WILLIAM ABRAMOWITZ: I asked Dr. Cornell to present this case again because a few members doubted the diagnosis. One even thought that it was an ordinary case of alopecia areata. The slow onset, the typical picture of

"gulfs and promontories," the permanent loss of hair and the presence of atrophy conform to the classic description of this disease, first given by Brocq. This condition of the scalp is entirely different from folliculitis decalvans because of the clinical absence of any follicular involvement in pseudopelade. Further, the histologic picture of folliculitis decalvans shows a plasma cell infiltration, entirely absent in pseudopelade (see recent monograph by Photinos on pseudopelade).

DR. ISIDORE ROSEN: I do not believe that pseudopelade and folliculitis decalvans are one and the same disease. Although they both end in atrophy and permanent alopecia in the involved areas, the lesions of folliculitis decalvans are follicular pustules ending in atrophy and scarring, whereas in pseudopelade there are no pustular lesions. There may be slight erythema which preceded the alopecia and atrophy. The lesions are much larger and are often mistaken for alopecia areata.

DR. OSCAR LEVIN: I think all the confusion concerning folliculitis decalvans and pseudopelade exists because of the fact that most textbooks have failed to classify them properly. They are two distinct diseases. In folliculitis decalvans there are inflammatory follicular papules and pustules pierced by hairs with firmly adherent crusts which, when removed and when the lesions heal, leave depressed scars. The aggregation of these scars results in the formation of cicatrical alopecia. In pseudopelade we have an entirely different condition. In this disease there is a superficial redness of the scalp which spreads along the surface of the scalp not showing a definite relationship to the hair follicles and resulting in the formation of superficial, thin, atrophic, bald areas without any macroscopic evidence of folliculitis.

DR. VAN ALSTYNE CORNELL: I believe that this is a case of pseudopelade, on account of the large, irregular bald areas pierced by a few long hairs. The skin over the lesions is white and glistening with considerable atrophy.

VON RECKLINGHAUSEN'S DISEASE. Presented by DR. ISIDORE ROSEN.

C. H., a girl, aged 17, born in Russia, called at the clinic of the New York Post-Graduate Hospital on Oct. 16, 1931, stating that her skin had been in the condition which then existed since birth. On the left cheek there was a large palm-sized area with mottled, brown, pigmented, macular lesions. There was a coin-sized *café-au-lait* spot on the right jaw. Various-sized similar spots were seen over the trunk. Over the right scapula was a bluish, flat lesion the size of a nickel, with a soft center and suggestive of herniation. There was a cherry-sized soft tumor on the left elbow. A similar tumor was seen under the left nostril. Over the back and arms there were many pin-point to pea-sized freckle-like lesions.

DISCUSSION

DR. OSCAR LEVIN: I agree with the diagnosis of von Recklinghausen's disease. In fact, it is a frank example of this condition. To the dermatologist these cases seem to be uncommon. However, it is my impression that such cases are frequently observed in neurologic clinics. The skin shows small and large fibromas, some showing myxomatous degeneration, pigmented lesions and nevi. The skin everywhere is dry and shows slight scaling and scattered hyperkeratotic follicular papules. There is no doubt that on further examination the patient will present evidences of endocrine disorder. It is my belief that these cases are associated with dysfunctions of the vegetative nervous system and the endocrine glands. I would suggest that the eyes be examined for tuberculosis.

DR. LOUIS CHARGIN: Do you consider this disease a nevus or due to some endocrine disturbance?

DR. ISIDORE ROSEN: This case emphasizes the importance of complete examination of all patients. The lesion on the face for which this patient consulted the clinic looked like a large pigmented nevus. Further examination disclosed

lesions on the trunk to substantiate the diagnosis of von Recklinghausen's disease. The blood cholesterol was found to be high. I also found a high cholesterol value in five other patients with von Recklinghausen's disease.

LICHEN PLANUS BULLOSUS. Presented by DR. B. M. JAMES.

F. W., a girl, aged 5, previously presented before the New York Dermatological Society by Dr. Fred Wise, had been admitted to the skin clinic of the New York Post-Graduate Hospital on Nov. 19, 1931. For the past five or six months the patient had had on the face, body and extremities pin-head to pea-sized erythematous slightly elevated papules some of which had been excoriated. Scratch marks were present on the body. The buttocks presented pea-sized papules, some in linear arrangement and some with a suggestion of pigmentation. The backs of the hands presented typical shiny, irregularly shaped papules which in places had coalesced, forming small plaques; on the backs of the fingers, these were violaceous. Some of the papules on the back of the hands were umbilicated. There was evidence of considerable scratching. The face presented smaller lesions, some of which were slightly erythematous. The lesions on the face were impetiginous. Biopsy confirmed the diagnosis of lichen planus.

DISCUSSION

DR. LOUIS CHARGIN: There is no question about the diagnosis of lichen planus in the case, but I doubt whether the large bullous lesion has anything to do with the lichen planus. It is not the type of bullous lesion seen associated with lichen planus. The bullae in this case are probably due to a drug or some external irritation.

DR. J. L. MORSE: I had the exact counterpart of this case a month ago in a man with generalized lichen planus who received mercuric salicylarsenate. As the lichen planus cleared up, bullous lesions such as this patient presents developed on the arms and legs. A biopsy of one of the bullous lesions did not show lichen planus. The bullous lesions cleared up under sodium thiosulphate. The urine of my patient was negative for arsenic, but I thought the eruption was due to the mercuric salicylarsenate. I feel the same in this case, that it is not bullous lichen planus but a drug eruption, although mercury rarely causes bullous lesions. I agree that the patient has lichen planus. A biopsy should be taken from the bullae.

DR. SAMUEL PECK: I asked the patient whether she had had any bullous eruptions before receiving treatment. She said that she did not have any. The bullous eruption appeared after she had received a number of injections of arsphenamine. I therefore agree with Dr. Chargin, that the bullae are secondary and probably due to injections of the drug.

DR. MAX SCHEER: In bullous lichen planus the bullae appear in the lichen planus lesions. Most of them are small papules. If they occur on patches they are limited to these patches and often have the irregular outline of the papules. In the case under discussion they have no such distribution. Furthermore there are no lesions of lichen planus. There is no evidence of external irritation (erythema); this negative feature plus the history of taking medicine for headaches suggests the probability of a drug rash.

DR. E. WILLIAM ABRAMOWITZ: Do the members agree that the patient had lichen planus?

DR. PAUL GROSS: I would like to suggest another diagnostic possibility, i. e., epidermolysis bullosa, with the formation of epidermal cysts. On examination the lesions greatly resembled lichen planus, but on closer inspection one could see only somewhat elevated lesions with pinhead-sized white inclosures under the skin, which could be interpreted as milia-like formations. The mother volunteered the information that the eruption began with blisters on the knuckles, back of the hands and elbows, and that they developed especially when the child knocked

against objects. I do not care to offer this diagnosis with any certainty, but if the condition does not respond to therapy for lichen planus, I believe it worth while for consideration.

DR. OSCAR LEVIN: When I saw the patient at a distance, I made a diagnosis of epidermolysis bullosa hereditaria. The appearance of the lesions on the backs of the hands, especially over the knuckles, suggested the shiny epithelial cysts that one sees in that condition. However, on closer examination, I observed that the lesions were distinctly those of lichen planus. Some of the small discrete lesions suggested psoriasis. However, on scratching the lesions, the typical shiny scales and the bleeding points, characteristic of psoriasis, were found to be absent. There is no doubt in my mind that this is a case of lichen planus.

DR. DAVID BLOOM: There is a typical annular lichen planus lesion below the right elbow.

Subsequent histologic examination revealed the microscopic appearances of lichen planus bullosus (reported by Dr. D. L. Satenstein).

BROMODERMA. Presented by DR. C. A. GREENHOUSE.

N. K., a girl, aged 10 years, born in the United States, of Jewish parents, stated that about six months before presentation convulsive seizures had developed which had recurred several times since then. For the past five or six months the patient had been receiving bromide medication. The eruption had appeared during the past three weeks.

The lesions were confined to the legs, showing two patches the size of a dollar on the inner side of the left leg and one lesion the size of a half-dollar on the middle of the right shin. Large pea-sized papular lesions were scattered over the rest of the right leg. The large plaques showed a liver-red halo with central crusting and pustulation. The smaller lesions were of a similar nature.

The patches tests were negative for bromides, phenobarbital and solution of potassium arsenate.

SARCOID IN A NEGRO WITH ANERGY. Presented by DR. MARION B. SULZBERGER.

T. C., a Negro, aged 60, in good general health, was first seen at the clinic of the New York Post-Graduate Hospital on Aug. 17, 1931. He presented on the left ala nasi a dime-sized indurated mass composed of several irregular nodules from the size of a pea to that of a bean. The entire growth was partially movable en masse. Under the left lower eyelid and attached to the skin was a small egg-sized tumor, less indurated than the one on the nose and composed of pea-sized, ill defined, soft nodules. A bean-sized similar lesion was present in the lateral border of the left lower eyelid. These lesions had been present about three years and were growing progressively larger. They had not been painful.

There was a history of several of the patient's children having died in childhood of tuberculosis.

Repeated Wassermann tests proved negative. Smears for tubercle bacilli and Hansen's bacillus were also negative. Tuberculin tests in all dilutions, from 1:1,000,000 to 1:5,000, showed no reaction.

A biopsy report demonstrated the naked epithelioid tubercles typical of sarcoid. The lesion on the nose was excised in toto, and the other lesions were receiving roentgenotherapy. Roentgenograms of the bones and lungs were to be made and reported on later.

ACNE VARIOLIFORMIS (?). Presented by DR. EUGENE TRAUB.

The patient, N. F., was a man, aged 26, white and single. Twenty-one years prior to the present admission to the Stuyvesant Square Hospital clinic, the patient had been vaccinated. Three days later, a pustular eruption appeared on the arms and legs. These lesions became crusted and then disappeared, leaving

scars. New lesions appeared in crops. Fifteen years prior to presentation, similar lesions had appeared on the scalp, face and trunk, following an attack of dermatitis venenata.

Twelve years prior to presentation, the patient had been seen in the Stuyvesant Square Hospital clinic, where a diagnosis of tuberculosis of the skin was made. A Wassermann test was reported as negative. Biopsy showed a necrotic tuberculid.

About nine years prior to presentation, vision had become poor in the right eye. The patient went to the University of Pennsylvania, where a diagnosis of acne varioliformis was made. Biopsy showed no indication of tuberculosis. About seven years prior to presentation, Dr. Stokes made a diagnosis of acne necrotica.

During the last eight years there had been fewer new lesions. For two years there had been ulcers on the pubis, penis and scrotum, and in the natal cleft. The penis and scrotum had been swollen and there had been dysuria. There was almost complete loss of vision in both eyes one year prior to presentation. The patient had been under treatment, and vision had improved considerably.

The Wassermann test had been negative on repeated occasions.

The Patient's family history revealed the fact that the father had been totally blind for four years and had a four plus Wassermann reaction. The mother was living and well. The patient had one sister living and well who had been vaccinated at the same time as he had, and who had had a similar condition lasting about four months and ending in complete recovery.

Arsphenamine Dermatitis, Fixed Type. Presented by Dr. Louis Chargin.

J. C., a man, aged 30, a clerk, married, stated that in addition to the usual illnesses of childhood he had had typhoid fever in 1915 and malaria in 1918. Following treatment for the malaria with quinine, the patient stated that he had had a generalized itching eruption.

He had a syphilitic infection dating back twelve years. He had received no treatment during the first ten years. Because he had pains in the head and legs, he had a blood test taken which proved to be positive. He was placed on bismuth and arsphenamine. Following the third injection of arsphenamine a generalized eruption of the multiform erythema type developed, which cleared up in about two weeks. Six months later the patient was admitted to the Mount Sinai Hospital clinic. Because of the history of an arsphenamine dermatitis the patient was treated at first only with bismuth. About a year prior to presentation, treatment with neoarsphenamine was attempted. The patient took the treatment very well, and no skin eruption was observed until the sixteenth injection of neoarsphenamine. Following that, a series of small erythematous lesions developed on the hands and penis. At each of these subsequent injections the eruption, which was fixed in type, recurred.

At the time of presentation, the eruption consisted of pigmentations in small areas. Five lesions were present on the palmar aspect of the left hand, and two were on the fingers of the right hand. On the glans penis and the shaft of the penis there were several confluent lesions.

The patient denied taking either phenolphthalein or antipyrine.

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## PHILADELPHIA DERMATOLOGICAL SOCIETY

J. P. Guequierre, M.D., *Secretary*

*Jan. 8, 1932*

Jacob M. Schildkraut, M.D., *Presiding*

A Case for Diagnosis. Presented by Dr. Sherman for Dr. S. S. Greenbaum.

N. P., a man, aged 42, a laborer born in Russia, was sent to the syphilis clinic of the Philadelphia General Hospital with a diagnosis of psoriasiform syphilis.

The patient showed an erythematosquamous eruption, not itchy; there were large areas on the trunk that were not affected. The rash was limited largely to the upper and lower extremities, with involvement of the ears and eyebrows. On the lower extremities the rash was a mottled pink, with moderate scaling of the lamellar type. An eruption of red lesions the size of a pinhead and slightly larger and more numerous on the thighs than on the legs was present. The entire back showed a similar scaliness on a pinkish background. On the arms there were numerous red punctae in addition to the scaliness. Similar palm-sized patches (four or five) occurred on the chest.

The patient gave a history of having been well until seven years previously, when small lesions similar to the present ones appeared on the face, arms and thighs. A physician in New York told him that he had syphilis, although apparently no examinations of the blood were made. Sixteen injections were given into the calf muscles and later treatment with light. The rash healed while the patient was being given light therapy, but it recurred after this treatment was discontinued. For the past six years he had not received treatment of any kind.

The patient was in good health, except that he had lost his appetite. On exertion or on exposure to the sun he perspired freely, but almost entirely from the head. Longer exposure to the sun produced exhaustion from heat, whereas previous to the development of the rash he was never so affected. He was a laborer and when employed usually worked outdoors. He was not married. The family history was meager. He left his family in Russia when a boy. He could not recall the occurrence of a similar rash on any other members of the family.

In addition to the rash the patient showed acrocyanosis of both extremities. Both his arms and legs, especially when in the dependent position, showed marked cyanosis and felt cold to the touch. There was no subjective feeling of coldness, pain, numbness or symptoms of any kind. He had had his attention called to this condition a long time before, but could not tell for how long a period he had been suffering from it, or whether it occurred at the same time that the rash developed.

There was a small scar on the corona, the result of a lesion that had appeared four weeks previously. This lesion gradually healed spontaneously. He had a 4 plus Wassermann reaction.

DISCUSSION

DR. F. D. WEIDMAN: While I cannot offer a positive diagnosis, I think that some possibilities at least ought to be mentioned. There are essentially areas of atrophy, extensive and diffuse, and in many places they are rather reticulated by elevated lines corresponding to intervals between atrophic spots. Interposed between these areas there are erythematous swellings; they may be regressing papules. I think that perhaps the closest diagnosis I can make is poikiloderma atrophicans vasculare, and perhaps the streaking on the insides of the elbows strengthens that diagnosis. There are a number of definitely scaly papules that I cannot quite reconcile with poikiloderma, but I do not know that one could reconcile them with any of the alternative diagnoses. The condition is not angioma serpiginosum; it is not scleroderma.

DR. C. S. WRIGHT: I agree with Dr. Weidman that the most probable diagnosis is poikiloderma vasculare atrophicans. I have never seen a case, so that I am perhaps a little forward in saying that, but I heard Dr. Lane's paper on the subject some years ago, and I recall the description of the vascular lesions, which are more or less like these, although more extensive, and there certainly is an atrophic process here. Another feature is chronicity. I can offer no other suggestion as to diagnosis.

DR. S. S. GREENBAUM: I am a little loath to accept the diagnosis of atrophic vascular poikiloderma. We could not get a history as to the therapy given; all the areas have numerous telangiectatic spots, and on the lips and eyelids there are also a number of these telangiectases or flat angiomas. It may be that

excessive roentgen radiation was given. I do not know whether in poikiloderma vasculare there is such marked scaling as is present in this case. He had telangiectatic spots or angiomas on the penis also. One thought that I had was that in spite of the history of only seven years' duration this condition might be a form of ichthyosiform erythrodermia, although it does not look like any I have seen. However, I intend to take sections, and perhaps we will present him again next month, with more data.

DR. J. V. KLAUDER: I think that the telangiectatic form of lupus erythematosus should be considered.

DR. E. F. CORSON: I think that Dr. Greenbaum's objections to the opinion of the earlier speakers was not out of the way at all. Poikiloderma does look like an x-ray burn. I saw a case of this condition at a meeting in New York, and in many ways it resembled third degree or marked second degree x-ray burn. I think that the scaly lesions are early portions, transition forms between the erythema which is the beginning and the atrophic scarring which is the end, but the telangiectasia in the case presented struck me as being similar to the condition in Dr. Lane's case.

A CASE FOR DIAGNOSIS. Presented by DR. J. D. MORGAN.

A white boy, aged 3 years, was brought to the Skin and Cancer Hospital in June, 1930. He presented flat, purplish papules arranged in patches on the neck and left arm. A diagnosis of papillomatous nevi was made. A biopsy was performed and a diagnosis of basal cell carcinoma made. However, as the diagnosis did not seem to fit in with the clinical picture, this was recently checked over and the diagnosis changed. At birth the child was normal, except for a few small pigmented areas in the region of the spine.

When the patient was about 7 months old he spent a day on the beach, wearing a low-necked, sleeveless dress. The next day a mild sunburn developed, and the mother believed that the condition on the neck and arm developed following this.

The principal treatment had been that given with low voltage roentgen rays, but a few patches were treated with radium. In 1930, the area was spreading rapidly, but after the first intensive roentgen treatment, it seemed to be checked; and for a while the patches became more discrete; however, the reddish discoloration had been slowly spreading over the original area and had not receded.

Several intense roentgen treatments were given. For instance, in October, 1930, an 80 per cent erythema dose was administered over the neck, an aluminum filter 2 mm. in width being used. Two weeks later, with the patient under a general anesthetic, a full erythema dose was given over all the lesions except those on the neck, where the other treatment had been given. In February, 1931, an 80 per cent erythema dose was given over all the lesions, a filter 1 mm. in thickness being used; three months later this treatment was repeated over the whole area. Two and one-half months later a 75 per cent erythema dose was given without a filter; in last October, 1931, a 75 per cent erythema dose through a 3 mm. aluminum filter was given. These treatments had checked the spread and altered the appearance of the lesions somewhat, but it did not seem to be checked entirely, as some papillomatous areas appeared. The presenter felt that roentgen treatments had been given almost to the limit. After the first treatment there was a good deal of desquamation, but the area healed immediately, and there had been no more desquamation.

DISCUSSION

DR. J. V. KLAUDER: This is a most extraordinary case. Is the lesion a benign or a malignant melanoma? Dr. Morgan tells us that improvement occurred following intensive roentgenotherapy. I have never seen a benign melanoma dis-

appear following roentgen or radium therapy unless it was destroyed as part of a radiodermatitis. There are no nodular lesions that one would expect in malignant melanoma. I think that the raised chocolate-colored plaques are suggestive of a malignant condition. On the other hand, the age of the patient, the time of onset of the condition—in infancy—and the duration suggest a benign lesion. If it is malignant, it is relatively benign. In view of the uncertainty as to whether the lesion is malignant, I think that one is justified in removing sections from different areas for further histologic study. If a malignant melanoma can be diagnosed, I agree to the continued use of heavily filtered roentgenotherapy.

Dr. F. D. Weidman: I think that clinico-dermatologically this condition is a papillary nevus, but it is not one of the extremely well developed nevi. It could be nevus unius lateris. Some of the papules are pigmented; some are not. Some of the latter are translucent. In addition to the smaller, less conspicuous papules there are others causing us more concern: the translucent, rosier ones, with a suggestion of telangiectasis on them. If it were not for these translucent lesions, the condition would fall into the category of simple pigmented papilliferous nevi. The sections show a picture almost identical with that seen in the well known raspberry type of pedunculated mole, a rather broad pedicle with the surface divided into cotyledonous areas. I have sections of that sort that were removed from a man in his twenties, who had had them for ten years, in which the histologic features were those of carcinoma. I have shown these sections to my friends in the pathologic department, who agree that morphologically the appearances are those of carcinoma. I now ascribe most value to the clinical features in such cases. Thus, in a nevus one is dealing with embryonal cells. In the final analysis, the histologic diagnosis of cancer depends on embryonal qualities in the cells. If one is dealing with something one already knows is embryonal, one cannot seize on its embryonal qualities to bolster up a diagnosis of malignancy. One has to consider the invasion of the corium; experience teaches that the level of the sweat glands is seldom reached in ordinary benign nevi. Furthermore, much depends on what kind of lesion was selected for biopsy in this patient. I do not know whether or not this section was taken from the translucent lesions. If it was, I should say that the condition was not malignant clinically.

Dr. Summerill: These sections were taken about a year and a half ago, when my predecessor called the condition basal cell epithelioma. As I felt assured about the diagnosis of melanoma when I saw the same sections, we considered it inadvisable to perform another biopsy on account of trauma, which is to be avoided in this type of growth.

Dr. J. D. Morgan: I was away when the biopsy was performed, but when I first saw the patient there were a few translucent areas, and I presume that one of them was removed because it would be the most obvious thing to take. These areas have been present from the time we first saw the patient, but they are more numerous now.

Dr. F. D. Weidman: I do not think that this condition is malignant. There is another interesting item; a spot appeared over the sacrum at birth. When there are congenital cutaneous manifestations there may be, among others, spina bifida; in all such cases it is well to examine the condition of the spine roentgenologically. Sometimes there are large tufts of hair over such spinal defects. Some of the extensive cases have been known to be associated with pigmentary nevoid changes in the entire cerebrospinal meninges; the presence of neurologic symptoms in the child is a point to consider.

Dr. Summerill: The growth of these nests of cells, removed a year and a half ago, occurred in the surface epithelium, and the numerous sections I examined showed little evidence of their breaking through the basal layer and extending into the corium. Of course, at the time this would have been encouraging, but now further extension is not in evidence. I consider that these nests of cells have characteristics of malignancy. There is a variation in the quality of the nuclei

that is confirmatory. There are variations in size, shape and chromatin content, and some of the cells are multinuclear. I have always found a growth of this type of nevus fundamentally greatly deceptive as to the evidences of malignancy. In one case a primary lesion on the leg recurred after supposed removal by another physician about a year before. I obtained the sections made at autopsy, and the tiny growth, only a few millimeters in diameter, did not show any suggestion of malignancy. However, the metastases were so extensive as to cause death soon after the endeavor to remove the lesion by minor surgical intervention. It is regrettable that the correct diagnosis in the case that is being presented was not recognized a year and a half ago, when the growth was far less extensive, for then the prognosis would have been far more assured.

DR. S. S. GREENBAUM: I think that the clinical picture and the photographs are definitely indicative of melanocarcinoma. I also feel that roentgen rays and radium are never to be used in the treatment of pigmented nevi, as I believe that they stimulate them. I do not know whether that treatment had such an effect in this case, but when the original photograph is compared with one taken a year later, nodulation is noted through an area where it was not present before. If this were my child, I should use extensive excision by the electrothermic knife, followed by plastic surgical procedures later. In my opinion, the prognosis is exceedingly grave.

DR. SUMMERILL: The appearance of these nests of cells in the epithelium is concurrent with earlier suggestions that melanomas are of epithelial origin. I do not believe that even in this case the condition is of epithelial origin, but I hold that it is in accord with Masson's statement about five or six years ago that the lesion is made up of embryonal cells of neuro-ectodermal origin or of possible glial nature. Even though in this case, the nodules are completely within the epithelium of the skin, the nests of cells are probably embryonal and associated with the formation of sensory end-organs, and I still believe, although there is nothing in the literature to substantiate this, that the growths are probably of glial origin.

DR. W. O. ROOP: When Dr. Weidman discussed this case, I was sorry that he did not make some suggestions for treatment.

DR. F. D. WEIDMAN: I am not in a position to advise about treatment, but at the Oncologic Hospital, where patients with rodent ulcers in the late stages come for treatment, plastic surgery has accomplished remarkable results. I am in accord with Dr. Greenbaum about the use of roentgen rays. Whether the condition is malignant or whether merely good cosmetic results are desired, the plastic surgeon could produce a satisfactory appearance.

I particularly asked about the lesion from which the section was taken, because my first impression of these translucent nodules was that there was perhaps a secondary lymphangiomatous development, which we all know sometimes takes place in a more or less zosteriform distribution like that of these lesions. If it were found out that the composition of one of these translucent nodules was lymphangiomatous (circumscriptum), of course that would be very comforting in the prognosis, and perhaps would clear up a great deal of uncertainty in the case.

DR. J. V. KLAUDER: In view of the age of the patient and the extensive area of involvement, I do not believe that it is advisable to attempt treatment by electrodesiccation.

DR. J. D. MORGAN: When I first saw the condition in September, 1930, my first feeling was that the lesions were nevi, and they did not seem to show the pigmented qualities seen now. We received the report that it was a basal cell condition at that time, and, being so extensive, I thought that it would respond well to roentgen ray treatments. After two treatments had been given, the sections were reexamined, and we received the report that the reaction was not that of basal cell lesions; that is why we requested another pathologic opinion, and I felt

like Dr. Klauder, that in a child a little over a year old the process was very extensive, since it denuded so much surface, and that treatment should be administered far enough beyond the area involved to assure thoroughness of treatment. At the rate at which the condition was spreading when I first saw the patient, treatment would have had to extend beyond the area seen to be affected to insure cure. If the condition is as malignant as appearances seem to indicate, the extraordinary feature is the fact that the boy continues to flourish and grow and shows no signs of metastasis.

DR. S. S. GREENBAUM: I merely want to add that I certainly should not continue to administer radiation. When there is a melanocarcinoma of an extremity, that extremity is amputated. If one waits for metastasis, one had better start writing the death certificate; now is the time to treat the condition if any results are to be obtained.

A CASE WITH A TENTATIVE DIAGNOSIS OF TUBERCULOSIS CUTIS. Presented by DR. PILLSBURY for DR. JOHN H. STOKES.

A colored boy, aged 12 years, presented a chronic granulomatous process involving the region above the bridge of the nose, the right eyelid and the right cheek. The scars of surgically drained suppurative lymph nodes were present over the anterior cervical chain. The lesions on the face were soft, raised and brown, and showed no contractile scarring. The lesion on the right eyelid extended across the entire lid and was 4 mm. in width. There were several sinus openings, but they could be probed for only a short distance. No pus could be obtained from the lesions when first seen. A section taken at biopsy from the lesion on the right cheek showed many giant cells, an intense infiltrate of round cells in the lower part of the corium, but few endothelial cells and no free pus. No blastomycetes were visible. Roentgenograms of the region of the frontal sinuses and of the chest gave negative results. The Kolmer and Kahn reactions of the blood were negative.

The process started three years before presentation following a fall in which the patient struck the region above the bridge of the nose. The lesion became suppurative, and a piece of bone was removed. The lesions on the right eyelid and the right cheek and the suppurative lymphadenopathy developed successively. The mother stated that these lesions were markedly suppurative.

DISCUSSION

DR. F. D. WEIDMAN: I saw the sections this afternoon, and I think that the entire absence of suppuration excludes blastomycosis and sporotrichosis, as was surmised clinically. This is not clinically or histologically an essentially suppurative condition. The sections show no epithelioid cells but an extraordinary number of giant cells. I feel that this is due to a tubercle bacillus of a low grade of virulence. Perhaps clinically the condition might be classified as sarcoid, although the involvement of the neck would make such a classification difficult. This case might be an interesting approach in point of virulence—a bridging case between sarcoid and a viable tubercle bacillus infection in which the particular strain is yet of very low grade of virulence. I think that in the future we will have to pay more attention to the factor of virulence in the tubercle bacillus (S, R, O and G colonies, etc.). Bacteriologists are working intensively on that phase of tuberculosis now.

DR. S. S. GREENBAUM: I should like to say that I agree with Dr. Weidman. We will have to change our ideas concerning the tubercle bacillus, its methods of reproduction and its life cycle, and it may be that various life forms of the tubercle bacillus produce different types of cutaneous tuberculosis. The condition in this case looks to me like a form of tuberculosis.

## MANHATTAN DERMATOLOGIC SOCIETY

M. B. PAROUNAGIAN, M.D., *Secretary*

*Jan. 12, 1932*

GEORGE M. MACKEE, M.D., *Chairman*

URTICARIA PIGMENTOSA NEVIFORMIS? Presented by DR. FRED WISE.

S. G. H., a boy aged 2½ years, from the Post-Graduate Clinic, presented a lesion, of approximately seven months' duration, in the right cubital fossa. The lesion consisted of a roughly circular plaque, barely elevated, one half by three-quarters of an inch (1.27 by 1.9 cm.) in diameter, of a dark fawn color, smooth surface and slightly palpable infiltration. The color was similar to that seen in the xanthelasmoidea type of urticaria pigmentosa. There were no other lesions, and subjective symptoms were absent. The mother stated that the lesion was slowly enlarging. Vigorous rubbing of the lesion did not produce an urticarial reaction. Biopsy was not permitted.

DISCUSSION

DR. GEORGE C. ANDREWS: I agree with the diagnosis as presented. The nodular lesion did not form a wheal when it was rubbed, but it might at another time. The yellowish color is characteristic. I treated a patient with a similar case—a localized, nodular type of urticaria pigmentosa, the diagnosis of which was proved by microscopic examination—with a suberythema dose of radium. The lesion disappeared and never recurred.

DR. DAVID L. SATENSTEIN: The lesion was raised, irregular yellowish-brown, firm and adherent to the cutis proper. It was present before the child had taken any medication. To me, it did not have any of the characteristics of a phenolphthalein eruption. I favor some form of a yellowish nevus, the exact nature of which can be established only by microscopic study.

A CASE FOR DIAGNOSIS (ERYTHEMA MULTIFORME, RESEMBLING DARIER'S DISEASE?). Presented by DR. G. C. ANDREWS.

Peter J., a white boy aged 7, gave a history that there had been no previous cutaneous disease except mild eczema during infancy. The patient was admitted to the Vanderbilt Clinic on Jan. 6, 1932, for otitis media of both ears. He was treated for this condition and also for a polyp of the left ear. After the ears had stopped draining, an eruption developed on the skin, and the patient was referred to the dermatology department. At that time he presented a more or less generalized eruption of one week's duration, with sudden onset. He had had no fever, malaise or medication. Physical examination showed a diffuse, papular, keratotic eruption on an erythematous base, scattered irregularly over the palms, knuckles, flexor surfaces of the arms, dorsum of the feet, face and ears. On the face there was a spot the size of a quarter which had the appearance of psoriasis. There were also psoriatic spots on the extensor surfaces of the forearms. The throat revealed a slight irritation on the right side. A specimen of tissue was taken for biopsy on January 11, from the left arm.

DISCUSSION

DR. MAX SCHEER: The eruption followed purulent otitis media, and since it is eczematous, it suggests the diagnosis of infectious eczematoid dermatitis.

DR. DAVID L. SATENSTEIN: Erythema multiforme is a process limited to the cutis. Darier's disease is a dry, primarily epidermic, process. The eruption

in this case was not uniform; in part it was inflammatory, in part keratotic, and in part both conditions were present. I should be in favor of a diagnosis of chronic follicular dermatitis with a secondary eczematous process due to the scratching.

DR. FRED WISE: The peculiar yellowish-pink tylosis of the palms and soles, together with the follicular keratoses and scaly patches on various parts of the body indicates that the eruption is in all probability pityriasis rubra pilaris.

DR. GEORGE C. ANDREWS: The variety of opinions that have been expressed have not helped to clarify the diagnosis. I hesitate to make a diagnosis of a chronic disease such as pityriasis rubra pilaris. In an eruption of only ten days' duration which is not typical there are no follicular papules on the backs of the proximal phalanges. However, the hyperkeratosis of the palms and soles suggested this diagnosis when I first saw the patient and before I examined him carefully. I am inclined to think that this is a toxic erythema of psoriasiform type.

NOTE: A subsequent report substantiated the diagnosis of pityriasis rubra pilaris.

A CASE FOR DIAGNOSIS (NEUROTIC EXCORIATION OR PICKER'S DISEASE?). Presented by DR. JOSEPH J. ELLER for DR. B. F. OCHS.

A. D., a girl aged 13, presented sharply punched-out lesions on the arms, the upper parts of the legs, the flanks and the buttocks. Many of these lesions had epidermidized, and presented characteristic pigmentation, while others, more recent, showed blood clots and acute inflammatory signs. On the buttocks, the lesions were very numerous and close together, while on the arms and back they were fewer in number. The disease was of about six months' duration. The patient admitted picking the lesions but did not say what she had picked out.

DISCUSSION

DR. ANDREW J. GILMOUR: I agree with the diagnosis.

DR. L. OULMANN: I regard the lesions as due to some form of tuberculosis of the skin, the condition which they most closely resemble being lupus miliaris. The condition needs more study.

DR. MARION B. SULZBERGER (by invitation): In this case it seems to me that a diagnosis of tuberculid—a rather superficial form of papulonecrotic tuberculid—must be considered. In favor of this are: (1) the age and sex of the patient; (2) the history of onset in a sudden manner; (3) the onset in the fall season; (4) the marked coldness and cyanosis of the hands and feet; (5) the predilection for localization on the extensor surfaces and on the buttocks; (6) the absence of wheals; (7) the absence of definite or marked pruritus; (8) the clinical appearance with lesions in different stages of development and regression, and the appearance and development of the individual lesion. They begin as a scarcely elevated, small, pea-sized papule, first reddish and then bluish-red; a crusting center then develops, and finally a flat, approximately round atrophic scar remains with slight surrounding pigmentation.

Dr. Ochs was kind enough to bring this patient to the Post-Graduate Clinic where I had the opportunity of testing her. The patient was anergic (hyposensitive) to tuberculin, not reacting to intradermal injection of old tuberculin Koch up to a concentration of 1:100! This is very unusual in a girl of this type and age, and shows an abnormal hyposensitivity to tuberculin. A finding such as this speaks in favor of the diagnosis I suggested, for Martenstein and Noll have found a relatively large percentage of papulonecrotic tuberculids to be anergic (see article by Sulzberger, M. B., and Wise, F.: Tuberculin: Newer Dermatological Considerations and Reasons for Its More General Use in Diagnosis, *M. Clin. North America* **14**:1555 [May] 1931). Of course more work must be done on this case. Biopsies of several lesions must be made, and inoculations into

guinea-pigs and cultures made. A thorough examination and roentgen study of the lungs should not be omitted.

Furthermore, the response to therapy must be considered. A possible response to injections of a gold compound or successful general antituberculous therapy would favor the diagnosis I suggest.

I believe that in Central Europe this case would be considered a type of papulonecrotic tuberculid clinically, and the investigations have so far also been in favor of this diagnosis. I have now seen relatively numerous cases resembling this condition in this country, have had the opportunity to make tuberculin tests and have frequently found them anergic in spite of an old case of tuberculosis of the lungs. None of these cases had previously been diagnosed as tuberculid, and I believe it possible that we do not make this diagnosis as frequently as we should.

In reference to this particular case I should like to add that the patient has markedly enlarged, doughy, indolent, anterior and posterior cervical lymph glands.

DR. MAX SCHEER: I do not think that this is a case of neurotic excoriations of the skin; there are no excoriations present now, though the patient admits occasional picking of lesions because of slight itching at times. The patient does not appear to be neurotic. The lesions show no necroses or pitted papulonecrotic tuberculid. But the remarkable type of reaction or rather lack of it to concentrated dilutions of tuberculin seems, as Dr. Sulzberger suggests, to put the case in the group of "anergic" tuberculids.

DR. MIHRAN B. PAROUNAGIAN: The clinical picture does not suggest tuberculid to me. I am inclined to agree with the diagnosis of neurotic excoriations. The mentality of the patient suggests that diagnosis.

SCLERODACTYLY SCLERODERMA AND SCLERODACTYLY. Presented by DR. H. J. F. WALLHAUSER.

A woman, aged 32, married, the mother of two children, both in good health, was referred from the dermatologic clinic of the Hospital of St. Barnabas, Newark, N. J., by Dr. J. W. Gardam. There was nothing unusual in her previous history. The results of the physical examination were negative. The laboratory findings, including the Wassermann and Kahn tests, metabolism test, urinalysis and blood count, were negative except for moderate anemia. The blood count showed 3,610,000 erythrocytes, and hemoglobin, 69 per cent.

The present condition began about four months before presentation with swelling of the distal ends of the fingers and gradual loss of the nails. Subjective symptoms consisted of coldness and numbness of the hands and feet, with intense pain in the fingers. The patient also complained of a general feeling of malaise; she "was tired all the time and nervous." Following the involvement of the fingers a gradual extension occurred, involving the arms, face, neck and chest, the skin becoming thickened and rigid, presenting a smooth glossy appearance of grayish color and areas of brownish pigmentation. The face presented the usual masklike expression, the fingers were semiflexed and rigid, and there had developed a feeling of constriction about the wall of the chest.

The patient came under observation about six weeks before presentation and was given a solution of ferric citrate mixture, 5 grains (0.325 Gm.), with corrosive mercurous chloride 1/32 grain (0.002 Gm.) three times a day, by Dr. McCauley—a mixture we had tried in other cases due to an apparent toxemia. Marked and rapid improvement followed, the feeling of malaise subsided, the skin in all affected areas gradually softened, the facial expression became normal, and the flexibility of the fingers, while not completely free, yet had improved sufficiently to permit her to return to work.

The case was presented on account of the remarkable improvement shown thus far. However, I realize the uncertainty of judging the outcome in this condition, and a further report is to follow.

DISCUSSION

DR. MAX SCHEER: The patient undoubtedly has scleroderma, but the relationship of the nodular lesions on the back to the scleroderma is uncertain.

SARCOMA; MELANOCARCINOMA. Presented by DR. MAX SCHEER.

Mr. S. L., about 70 years of age, retired, from the Post-Graduate Clinic had had the condition for approximately one year. On examination the patient presented a large, marble-sized ulcerated mass on the left hand, toward the radial (lateral) side, about ¾ inch above the metacarpophalangeal articulation of the first finger. The lesion was indurated and infiltrated. The surface was raised, granular and moist, and one small area showed a slightly bloody exudate. There was no adjacent, regional lymphadenopathy. There were darkish-brown, mottled pigmented areas with and adjacent to the ulcerated area.

DISCUSSION

DR. GEORGE C. ANDREWS: I think that the lesion is typical of melanoma. I also think that at an early stage the clinical diagnosis is often more reliable than the interpretation of the microscopic findings.

DR. DAVID L. SATENSTEIN: The clinical course of melanosarcoma is much shorter than that of melanocarcinoma. Patients with sarcoma do not live long.

DR. LOUIS B. MOUNT: I feel that if this case were melanosarcoma the patient would not be living. I agree that a malignant condition is present but it is not melanosarcoma.

A CASE FOR DIAGNOSIS (SEBORRHEAL ECZEMA OR BEGINNING PEMPHIGUS?). Presented by DR. MAX SCHEER for DR. B. F. OCHS.

M. T., a man aged 56, presented on examination a fairly generalized eruption on the back, chest, legs and upper part of the arms, the duration of which was about three months. The individual lesions varied in size from a pea to that of a coin. The lesions were slightly scaly and on a reddened base. Some of them showed crust marks and blood crusts, due to the itching. The patient complained of a good deal of burning of the skin. There was well marked seborrhea on the back of the ears and on the scalp. (The results of the examination of tissue taken for biopsy were reported as eczema.)

The patient was presented for diagnosis, with a tentative diagnosis of a seborrheal eczema or beginning pemphigus.

DISCUSSION

DR. FRED WISE: I think the condition is pemphigus vulgaris.

DR. MAX SCHEER: I believe that the eruption is pemphigus vulgaris. Dr. Ochs showed me the patient about a week ago when there was a dried bulla on the back.

ROSACEA-LIKE TUBERCULID. Presented by DR. FRED WISE for DR. MARION B. SULZBERGER.

Mr. J. P., married, aged 29, presented himself at the Post-Graduate Clinic on Dec. 31, 1931, for treatment of a papulopustular eruption of the cheeks and forehead. He had been treated with dietary regulation, roentgen rays (15¼ unit doses) and local applications of white lotion, without benefit.

The family history was irrelevant. The personal history revealed that the patient had had an anal fistula six years previously, which was considered a Koch bacillus infection, had been operated on and had been treated with ultraviolet radiation. Examination revealed a violaceous and scaly eruption of the forehead,

temples and cheeks, which did not affect the midportion of the face or the nose. There were crusted papules and small pustules scattered through these areas, varying in size from that of a pinhead to that of a lentil. Quantitative tuberculin tests revealed marked hypersensitiveness, the reaction being positive at a dilution of 1:1,000,000 old tuberculin Koch. The Moro test was definitely positive, as well as the patch test.

Biopsy did not reveal a picture that could be construed as that of ordinary rosacea, but as a picture of chronic and acute granuloma. The pulmonary picture was insufficient in pathologic changes to confirm a diagnosis of tuberculosis. Inoculation into guinea-pigs has been performed and will be reported on at a subsequent meeting.

DISCUSSION

DR. GEORGE C. ANDREWS: I agree with the diagnosis as presented and wish in addition to mention the small, pitted scars on the forehead.

DR. DAVID L. SATENSTEIN: In the specimen I examined I found granulation tissue of no special characteristics that would be of diagnostic value.

DR. MARION B. SULZBERGER (by invitation): No other diagnosis covers this case as well clinically. The atypical localization for rosacea and the unusual course (refractory to roentgen treatment et cetera) are in favor of the diagnosis suggested. The patient is extremely hypersensitive to tuberculin. He had a definitely positive reaction to 0.1 cc. of serum in a dilution of 1:1,000,000, intradermally. The Moro test applied to lesions on the forehead caused marked local flaring-up of the condition, whereas the control salve caused no reaction. An interesting feature in this case is the fact that the patch test made with tuberculin was strongly positive, an eczematous reaction grossly or clinically with small vesicles appearing at the site of the patch on unaffected skin forty-eight hours after application. I believe that this is the first reaction of this kind reported in this country, and until recently no attention to this reaction had been given in Europe. This test seems entirely analogous to the patch test with trichophytin. It is interesting to speculate on the products of the tubercle bacillus as the possible causes of eczematous dermatitis, and I believe that this reaction means that this possibility exists.

The histologic picture of the lesions on the forehead speaks rather in favor of tuberculosis, although nothing definite could be found in the short examination of the slides this afternoon. We are going to treat this patient with injections of a gold compound, and I hope Dr. Wise will be able to report the results at a subsequent meeting.

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## BROOKLYN DERMATOLOGICAL SOCIETY

A. M. PERSKY, M.D., *Secretary*

*Jan. 18, 1932*

B. B. BERKOWITZ, M.D., *Presiding*

LUPUS ERYTHEMATOSUS TELANGIECTATICUS. Presented by DR. A. WALZER.

C. P., a woman, aged 33, was first seen at the Good Samaritan Dispensary (New York) in 1922, with a large, dark, erythematous patch on the lower part of the right side of her face. About one month later, or six weeks after the onset of the disease, she was presented at the Section of Dermatology of the New York Academy of Medicine with a diagnosis of angioma serpiginosum (ARCH. DERMAT. & SYPH. **9**:507 [April] 1924). This diagnosis was not accepted

but dermatitis artefacta and hemorrhagic lupus erythematosus were suggested. The final diagnosis at the Good Samaritan Dispensary was hemorrhagic lupus erythematosus.

At a meeting of the Section of Dermatology of the Academy of Medicine on Nov. 1, 1926, about three and one-half years later, the patient was again presented as showing healed lupus vulgaris, treated with radiation from the Kromayer lamp and with the roentgen rays (the case is not reported in the transactions of that meeting).

The patient was not seen again until a few weeks prior to this presentation, when she came to the morning dermatologic clinic of the Brooklyn Jewish Hospital with the lesions as presented here. She stated that about two months before presentation she had her tonsils removed, and within a week a small patch appeared on her nose, which grew steadily.

On the tip of the nose was a patch the size of a twenty-five cent piece, erythematous, slightly elevated, infiltrated and without scaling. On close inspection it was seen to be made up of many fine dilated vessels and points. The center was depressed and atrophic. On the right side of the lower part of the face was a large, depressed wrinkled scar, the result of treatment. Along the border were a few scattered telangiectatic points. The outer portions of both ears showed flat, erythematous patches, composed of small dilated vessels. The rest of the skin was normal.

DISCUSSION

DR. A. WALZER: When this case was first shown in November, 1923, before the Section of Dermatology of the Academy of Medicine, a number of suggestions were offered as to the diagnosis. However, from the result of treatment and from the recurrence as shown here, the case unquestionably is one of telangiectatic lupus.

At this presentation, the patient showed a few telangiectatic points along the border of the old scar, indicating a lighting up of the old process. Was the form of treatment that this patient received advisable, or would it have been better to have left the condition alone, since it is known that in many of these cases healing eventually occurs spontaneously?

DERMATITIS HERPETIFORMIS. Presented by DR. WILLIAM H. BEST.

B. W., a married woman, aged 52, presented an eruption of about two and one-half years' duration. It first appeared on the abdomen as vesicles the size of a pea which appeared in crops. The eruption gradually spread until at the time of this presentation, the abdomen, chest and upper and lower extremities were involved. The rash from the beginning was accompanied by intense itching and burning. There have been no periods of remission, the patient becoming progressively worse.

Large areas of cutaneous surface were macerated and denuded of epidermis. Between the macerated areas were vesicles the size of a pea, in clusters, some showing a circinate arrangement. The vesicular patches were in various stages of evolution, from the new, tense lesions coming from an apparently normal integument to the flaccid and ruptured clusters surrounded by an inflammatory areola. There was considerable pigmentation at the sites of healed lesions.

Chemical examination of the blood, the Wassermann test and tests of the urine gave negative results.

DISCUSSION

DR. A. WALZER: This patient had been shown by me at the November, 1931, meeting of the Brooklyn Dermatological Society as presenting a "Case for Diagnosis." At that time the diagnoses of pemphigus, multiform erythema and bullous urticaria were suggested. Her condition now is very much worse than it was at the last presentation. Is is possible that the taking of drugs (quinine, phenobarbital, arsenic, etc.) as her hospital chart shows, may be responsible for some of her present condition?

DR. J. SKEER: The patient came to the United Israel Zion Hospital Dispensary two and one-half years ago with a markedly pruritic papulovesicular eruption on the chest, abdomen and back; it was thought to be scabies or a beginning dermatitis herpetiformis. The bullae appeared flaccid and not tense and were situated superficially on the skin. After the bullae disappeared, dry, red skin remained. It seemed that some of the bullous lesions had an umbilication in the center, and my diagnosis would be erythema multiform bullosum or pemphigus.

PARAPSORIASIS EN PLAQUES. Presented by DR. J. SKEER.

S. G., a woman, aged 39, came to the Jewish Hospital complaining of numerous "spots" on the chest, abdomen, back and limbs.

Five years before presentation the patient noticed a bluish lesion on her back and left leg, which increased in size and spread to the other areas. Two years ago she went to a New York clinic where her condition was diagnosed as "scleroderma." The patient was treated and received numerous injections of sodium thiosulphate.

There were numerous brown areas of hyperpigmentation the size of a dime situated on the chest and back and on the flexor surfaces of the thighs, legs and arms. Some of the lesions showed enlarged capillaries with glistening atrophic areas. There was no infiltration. The Wassermann test of the blood and chemical examination of the blood gave negative results.

DISCUSSION

DR. J. SKEER: Dr. Chargin in his description mentioned everything except the slight infiltration and sclerosis. Otherwise I believe the picture fits in very well with parapsoriasis en plaques.

The eruption began with a lesion on the posterior surface of the left leg and one area on the chest, and in a short time the rest of the pigmented areas appeared. At no time did the patient complain of itching.

A report of the biopsy will be ready at the next meeting.

A CASE FOR DIAGNOSIS (LUPUS ERYTHEMATOSUS?). Presented by DR. A. WALZER.

J. J., was a man aged 52 and married. There was no history of tuberculosis in the family and no history of the ingestion of drugs.

About four months prior to presentation a small red, elevated area appeared on the right cheek near the nose and it gradually spread peripherally. The lesion on the left cheek was of one month's duration. On the right cheek was an erythematous patch larger than a silver dollar, serpiginous in outline, with a sharply elevated border which was apparently made up of distinct portions. The center of the patch was somewhat depressed and lighter. On diascopic pressure, the erythema disappeared completely. On the left cheek was a smaller red area the size of a dime with a somewhat depressed center, which according to the patient was also increasing in size. There were no lesions on the rest of the body. The mucous membranes of the mouth showed brownish pigmented lesions.

DISCUSSION

DR. A. WALZER: I showed this case because there are three possible diagnoses: first, lupus erythematosus; second, sarcoid of Boeck, and third, an erythematous patch as an indication of some intoxication, due to drugs, etc.

Since there was no history of the use of drugs, the last diagnosis can be ruled out. Whether the condition is sarcoid of Boeck or lupus erythematosus may be difficult to determine clinically. Etiologically, however, the diseases are both tuberculous. The peculiar extension of the lesion, the formation of at least a

slight prominent border and the absence of atrophy may be present in either instance. Only by microscopic study can a distinction be made.

DR. L. CHARGIN: Syphilis should also be ruled out.

DR. A. WALZER: A Wassermann test was negative. There was nothing in the history that pointed toward a syphilitic infection.

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## DETROIT DERMATOLOGICAL SOCIETY

H. J. PARKHURST, M.D., *Reporter*

*Regular Meeting, Jan. 19, 1932*

EMMETT C. TROXELL, M.D., *Vice President, Presiding*

ALOPECIA TOTALIS. Presented by DR. ARTHUR E. SCHILLER.

A. McI., a Scotch schoolgirl, aged 13 years, had lost all her hair nine years before presentation, as the result of a fall on her head. All the hair had been lost within a month, and there had been no regrowth, excepting small, short, lanugo-like hairs, which were visible at the time of presentation. The Wassermann reaction was negative.

DISCUSSION

DR. GEORGE H. BELOTE: Recently we have begun to give an anterior lobe pituitary preparation intramuscularly and desiccated pituitary gland orally, as recommended for alopecia. Thus far we have observed no favorable results, but probably it is too early to judge.

DR. ROBERT C. JAMIESON: According to endocrinologists, enormous doses of pituitary gland can be administered without harm.

DR. LOREN W. SHAFFER: I have seen no untoward reaction after high doses, except perhaps slight depression. Pituitary is expensive.

DR. OSWALD M. GRUHZIT: I feel that large doses are not harmful. Treatment with this drug for alopecia is still experimental.

A CASE FOR DIAGNOSIS (SECONDARY SYPHILID OR DERMATITIS MEDICAMENTOSA [ARSPHENAMINE]?). Presented by DR. CLYDE K. HASLEY.

Mrs. D. O., before coming to the Grace Hospital Clinic, had received ten injections of neo-arsphenamine. An eruption had appeared on the arms, axillae and groins, and had soon become generalized, the face and lower parts of the legs remaining exempt. The lesions were maculosquamous, erythematous and ovoid, their distribution following the lines of cleavage of the skin; they had recently become violaceous and pigmented. The possibility of pityriasis rosea had also been considered. The Wassermann reaction had been negative at the clinic.

DISCUSSION

DR. LOREN W. SHAFFER: The pigmentation favors a diagnosis of an eruption due to arsphenamine, and the slow improvement following treatment with sodium thiosulphate confirms this diagnosis.

DR. GEORGE H. BELOTE: The distribution and shape of the lesions and the lesions on the back are suggestive of pityriasis rosea. The pigmentation suggests lichen planus, but the condition may be due to arsenic. Two of these conditions may be combined in this case.

DR. ARTHUR E. SCHILLER: I saw the patient previous to presentation; she had a typical arsenical eruption, with overlying scaly lesions that faded after exposure to ultraviolet rays and left the slowly fading, original eruption.

DR. ROBERT C. JAMIESON: The lesions on the neck have the appearance of a syphilid.

DR. CYRIL K. VALADE: I agree with Dr. Jamieson. Ultraviolet rays may have increased the pigmentation.

ADENOMA SEBACEUM AND NEVOID, SUBUNGUAL TUMORS. Presented by DR. CYRIL K. VALADE.

Mrs. P. C., a housewife, aged 35, had had cutaneous lesions for ten years and stated that her sister had had a similar condition. Under the free borders of all the toe-nails and some of the finger-nails, there were lesions, apparently fibromas, varying in size from that of a large pinhead to that of a small pea. Deformities of the nails were also present, especially dystrophy of the right great toe-nail. There were three groups of fibrous nevi on the trunk and a large coin-sized hairy mole below each patella. There were numerous pinhead-sized, erythematous lesions on the cheeks adjoining the nose. Roentgenograms were shown.

DISCUSSION

DR. ROLLIN H. STEVENS: Roentgenograms showed rarefied areas at the ends of the affected phalanges, probably due to the pressure of these tumors.

DR. GEORGE VAN RHEE: The lesions on the face are adenoma sebaceum. The others resemble nevi.

DR. HARTHER L. KEIM: The lesions on the nails may be related to the facial condition.

DR. WILLIAM G. SAUNDERS: Infection is said to have preceded the lesions on the fingers.

DR. HOWARD J. PARKHURST: I consider the condition a type of nevus.

NOTE.—This condition is apparently identical with that in the case presented before the American Dermatological Association in Toronto, by Dr. David King-Smith, Dr. E. J. Trow and Dr. H. A. Dixon (Adenoma Sebaceum: Nevoid Growths about Toe-Nails, ARCH. DERMAT. & SYPH. **25**:175 [Jan.] 1932).

PRURIGO MITIS (?). Presented by DR. CLYDE K. HASLEY.

M. N., a Negro boy, aged ten years, presented a generalized, small papular eruption, which had begun on the arms about five years previous to presentation. The lesions had appeared and disappeared in sucessive crops, and were accompanied by intense pruritus. The skin was dry, with pigmentation following previous lesions, and there were many excoriations.

DISCUSSION

DR. ROBERT A. C. WOLLENBERG: There were many tiny papules of keratosis pilaris on the abdomen.

DR. HARTHER L. KEIM: The lesions on the hands suggested scabies.

DR. ARTHUR E. SCHILLER: I suggest a trial of thorough treatment with applications of sulphur.

DR. WILLIAM G. SAUNDERS: I feel that this is not a case of scabies.

DR. HOWARD J. PARKHURST: The axillae are not involved, and there are papules on the extensor surfaces. I consider the condition prurigo mitis.

DR. LOREN W. SHAFFER: A therapeutic test is sometimes needed to differentiate between scabies and prurigo mitis, as in the present case.

A Case for Diagnosis (Epidermolysis Bullosa [?], Acrodermatite Continué [?]). Presented by Dr. Arthur E. Schiller, Dr. William G. Saunders and Dr. Clyde K. Hasley.

M. D., a boy, aged 11 years, had been presented before this society at the meeting of Dec. 15, 1931. He was again presented together with the specimens taken for biopsy for further discussion.

DISCUSSION

Dr. John A. Hookey: The histologic features are those of acrodermatite continué of Hallopeau.

Dr. Howard J. Parkhurst: Do the lingual lesions fit in with that diagnosis?

Dr. John A. Hookey: Barber found lesions of the mucous membrane in acrodermatitis.

Dr. Harther L. Keim: I have never seen anything to compare with this condition. The eruption is pemphigoid. The tongue looks pellagrous. Acrodynia can be excluded. Acrodermatite continué seems the most likely diagnosis.

Dr. George H. Belote: The lesions on the hands and feet especially remind one of acrodermatitis of Hallopeau. They might conceivably be epidermolysis bullosa, but that condition would not be so likely to involve the groins. I consider this condition severe acrodermatite continué.

Dr. Robert A. C. Wollenberg: Last month I considered the condition pemphigus, and I still consider that diagnosis correct.

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## PITTSBURGH DERMATOLOGICAL SOCIETY

Claude B. Norris, M.D., *Secretary*

*Regular Meeting, Jan. 21, 1932*

James H. Fiscus, M.D., *President*

Lupus Erythematosus. Presented by Dr. George J. Busman.

J. B., married, aged 20, presented a subacute, erythematous, squamous condition of the vermilion surface of both lips. There was considerable infiltration, such that the lips were rather prominent with scaling and follicular accentuation. The condition extended slightly below the mucocutaneous junction and onto the mucous surface; there was as well a questionable involvement of the hard palate. The lesion was very noticeable because of the intensely red color. The duration was three months. The Wassermann reaction of the blood was negative.

DISCUSSION

Dr. H. T. Phillips: I do not believe the disease was lupus erythematosus. The discoloration of the palms, which appeared at the same time as the disturbance of the lips, did not fit into the picture of lupus erythematosus. I could only say that it was a disturbance of pigmentation, the cause of which is yet to be determined.

Dr. L. G. Beinhauer: There is always a possibility of pigmentation, such as the patient presented, following the use of musical wind instruments and bismuth therapy. In lupus erythematosus, a peculiar bluish-white hue is present, especially on the mucous membranes, and this color was present in this patient.

DR. W. H. GUY: The diagnosis of lupus erythematosus did not appeal to me as applied to the lesions on the lips or on the hard palate. An unusual pigmentation was present on the lips, but this was of indeterminate source.

DR. H. G. WERTHEIMER: Although there was an unusual amount of bluish discoloration at the margins, the presence of white striae, color and slight scaliness led me to a diagnosis of lichen planus.

FRAMBESIFORM SYPHILID. Presented by DR. H. G. WERTHEIMER.

M. S., a girl aged 16, presented just below the middle of the lower lip, the chin and the left nasolabial sulcus a sharply defined, plateau-like area, the upper margins being rolled with central papillomatous excrescences. No other lesions of the skin were present. The Wassermann and Kahn reactions were 4 plus, and the lesions had improved slightly after one injection of oleo-bi-Roche. Examination for tuberculosis, blastomycosis and other conditions gave negative results.

DISCUSSION

DR. STANLEY CRAWFORD: I consider this lesion a warty type of syphilis due to secondary pyogenic superinfection, and not a true frambesiform type. This type occurs occasionally accompanied with perioral or perianal syphilids.

DR. J. H. FISCUS: This is the type that is seen occasionally in the Negro; it is rare in the white race. Secondary infection plays a prominent rôle in this type of lesion.

KERION. Presented by DR. LESTER HOLLANDER and DR. A. FISHER.

R. DeP., aged 49, presented on the left side of the upper lip a lesion of three weeks' duration, composed of many soft nodules from which sanguineous pus could be expressed. A culture of this was taken, but has not yet been reported on. The luetin and Wassermann tests were negative. An injection of trichophytin of 1:10 dilution gave a marked reaction, and the growth involuted considerably after this injection. Three other injections of trichophytin have been given since.

DISCUSSION

DR. CLAUDE B. NORRIS: The location of this lesion on the upper lip suggested to me a rather deep invasion of organisms derived probably from the nose. It is quite usual for a staphylococcic infection to be virile enough to produce more or less edema in an area such as the lip. There was some alopecia, and the hairs were fairly easily extracted. Of course, a tineal infection could produce all these phenomena, but, in the absence of demonstrable mycelia, I should be inclined toward a diagnosis of coccigenic sycosis. The influence of trichophytin in kerionic types I believe to be more or less nonspecific. The use of injections of whole milk, intramuscularly, in extensive, boggy kerion of the scalp is, as is known, frequently effective.

NEVUS. Presented by DR. J. W. BARR.

A. P., a schoolboy aged 9 years, white, presented, on Dec. 24, 1931, on the dorsal surface of the middle toe of the right foot, a rough, much infiltrated, purplish area, showing a number of rather closely set, deep-seated, translucent vesicles. The lesions had been present since he was a small baby, but had gradually become more extensive. One home physician advised that the lesion be curetted, and another, the removal of the entire toe.

DISCUSSION

DR. W. H. GUY: To my mind, this is a lymphangiomatous nevus. Removal is not indicated, but if insisted on could be done without the loss of the toe.

DR. STANLEY CRAWFORD: I consider the lesion a circumscribed fibrolymphangioma, and feel that if the lesion is painful, the toe might be amputated without any resulting disturbance. I suggested that trichloracetic acid be painted on the lesion every two weeks over a period of months.

DR. L. G. BEINHAUER: I should remove the growth surgically and apply a skin graft over the denuded area.

ERYTHEMA ELEVATUM DIUTINUM. Presented by DR. LESTER HOLLANDER and DR. J. J. HECHT.

Miss E. F., aged 17, had noticed during the past three winters several reddish, soft, erythematous tumefactions on the dorsal surfaces of the hands, especially around the knuckles. The Wassermann test showed: lipoid, negative, and cholesterol, 2 plus; the Kahn reaction was negative. Examination of the blood revealed: hemoglobin, 64; white blood cells, 7,400; red blood cells, 4,290,000; polymorphonuclears, 63; lymphocytes, 30; eosinophils, 1, and mononuclears, 6. The duration was three years.

DISCUSSION

DR. W. H. GUY: The patient stated that the condition appeared regularly two weeks prior to menstruation and disappeared with the beginning of the flow. This suggested a dysmenorrheic dermatitis of a pernio type.

DR. H. G. WERTHEIMER: I did not see any of the ringed eruption but, instead, a rose-colored, slightly elevated area on the fingers, suggesting a diagnosis of pernio.

DR. J. H. FISCUS: I believed this to be granuloma annulare.

DR. STANLEY CRAWFORD: I did not see sufficient clinical manifestations to make a diagnosis, but the one lesion on the right forefinger was suggestive of this condition.

DR. LESTER HOLLANDER: This was not a menstrual eruption, because it was present all the time. The lesions were very painful. One lesion in which definite nodules could be discerned was annular.

DR. J. J. HECHT: Dr. Sutton in his books calls erythema elevatum diutinum a synonym for granuloma annulare. He says that, histologically, the two conditions are either very closely related or the same. This patient's roentgenograms were negative for pathologic involvement of the bone. One of the characteristics of this disease is persistence. There was no history of rheumatism.

DISSEMINATE MILIARY TUBERCULOSIS. Presented by DR. GEORGE J. BUSMAN.

L. B., a colored woman aged 30, presented pinhead-sized, firm, glistening, scaly papules over the entire body. The lesions were all similar in character and of the same size. The palms and face were not involved. There were no lesions of the mucous membranes. The color was indefinite because of normal pigmentation. There were about a dozen lesions to the square inch on the entire body surface. There was moderate adenopathy.

The condition began in the spring, 1931, and at that time the Wassermann reaction of the blood was 4 plus. A diagnosis of lichenoid syphilis was made, and treatment was instituted. After a course of twenty-four injections of arsphenamine and sixteen intramuscular injections of bismuth there was no change in the cutaneous lesions. The Wassermann reaction of the blood reverted from a 4 plus reaction to negative.

A section of tissue removed for biopsy revealed typical epithelial and subepithelial granuloma characterized by an endothelial cell mass with caseation and early giant cell formation. Further study is being made to search for tubercle bacilli and other indications of tuberculosis.

DISCUSSION

DR. STANLEY CRAWFORD: I agreed with the diagnosis and considered this case a typical and splendid example of this type of tuberculosis in a Negro. I felt that this type was due to the spread of a nonbacillary form of tubercle bacilli in the cutaneous lymphatics, producing a lesion that often showed tubercle formation without central caseation of giant cells.

DR. HOWARD T. PHILLIPS: This case was an almost exact duplicate of two presented in Cleveland last year, in colored patients, as instances of disseminate miliary tuberculosis of the skin.

DR. B. A. GOLDMANN: The primary lesion was a papule, the surface of which became umbilicated and left a scar on healing. I should classify it as a papulo-necrotic tuberculid.

XANTHOMATOSIS (EDELMAN'S SYNDROME). Presented by DR. LESTER HOLLANDER and DR. FISHER.

Mrs. G. W., aged 41, American, white, a housewife, presented typical lesions of xanthoma tuberosum multiplex at the elbows, palms, buttocks and knees; xanthelasma-like lesions on the eyelids; general jaundice which was discernible in the conjunctiva, and an enlarged liver, the angle of which could be felt immediately above the brim of the pelvis. Roentgen examination showed that this was pushing the stomach downward to the pelvis. There were no bony changes in any of the skeletal structures.

This condition was of about four years' duration. There was nothing of importance in the history, except the fact that on account of some vague muscular pains the patient's teeth had been removed.

The laboratory examination showed the presence of bile in the urine, and strongly positive direct and indirect van den Bergh reactions. The cholesterol content of the blood on two examinations was 575 and 684 mg., respectively. A lesion was removed for biopsy, and the patient was placed on a fat-free diet.

The case was presented as one of Edelman's syndrome, because it seemed to fit the description as given by Weidman in his article on yellowing dermatoses.

DISCUSSION

DR. W. H. GUY: I agreed with the classification made by the presenters. The association of large liver, jaundice and xanthoma tuberosum multiplex was of particular interest in connection with the high cholesterol content of the blood. Sosman's article, which appeared recently in *The Journal of the American Medical Association*, could be reviewed with profit after seeing this case.

DR. L. G. BEINHAUER: This unusual case was similar to one I saw recently with jaundice, arthritis, tonsillitis and infected teeth. The lesions on the skin were less marked, and there were no lesions on the eyelids; on operation marked cirrhosis of the liver was found. Unfortunately, the patient died four weeks after operation.

DR. LESTER HOLLANDER: We presented the case, and should like to call your attention to Sosman's article (Xanthomatosis, *Am. J. Roentgenol.* **23**:581 [June] 1930), in which he classified xanthomatosis into three groups, the Schüller-Christian-Gaucher-Niemann-Pick syndrome, which shows bony changes and occurs in children, then xanthoma diabeticorum and finally xanthoma tuberosum multiplex, the latter occurring in adults.

DERMATITIS MEDICAMENTOSA (PHENOLPHTHALEIN?). Presented by DR. LESTER HOLLANDER and DR. FISHER.

R. S., aged 5, presented a generalized eruption affecting the entire body but principally the dorsal surfaces of the hands and the extensor surfaces of the arms and legs. The individual lesions were vesiculopapular. Some showed a central

depression. They left a slight superficial scar and a little pigmentation. Some showed a definite grouping. This grouping was especially noted on the lower extremities.

An interesting history associated with this eruption was as follows: The condition began after the patient had chickenpox in June, 1931, and since then had been more or less continuous. Whooping cough and measles had intervened since then. As the condition continued, a pediatrician gave the child a transfusion of blood in August. Since then topical remedies had been applied. The history also revealed that the patient had been given ex-lax and feenamint as laxatives.

The conditions to be considered are: (1) dermatitis medicamentosa, (2) lichen urticatus and (3) dermatitis herpetiformis.

DISCUSSION

DR. HOWARD T. PHILLIPS: This case seems to me to be one of lichen urticatus. I do not believe the condition is in any way associated with phenolphthalein.

DR. W. H. GUY: I saw this case before and obtained the history as related by the presenters. I felt that the condition was granuloma papulonecroticum.

DR. STANLEY CRAWFORD: I consider this a typical example of Bateman's lichen urticatus. I see no reason for considering the eruption due to phenolphthalein and think that we should avoid trying to attribute too many eruptions to this drug.

DR. H. G. WERTHEIMER: I should diagnose this case as one of lichen urticatus.

DR. J. H. FISCUS: Lichen urticatus is to be considered. The process is that of scabies.

DR. L. G. BEINHAUER: I believe that we are dealing with a toxic cutaneous eruption, presenting a necrotic papule leaving scars. I favor the diagnosis of papulonecrotic tuberculid.

DR. LESTER HOLLANDER: Lichen urticatus is the most likely possibility. This was mentioned in the presentation.

PHENOLPHTHALEIN ERUPTION? Presented by DR. STANLEY CRAWFORD.

H. L. S., a white man aged 45, a boiler maker, stated that four years prior to presentation bright red, rounded areas developed on the forearms. Within two days, similar areas appeared on the legs, thighs, trunk, upper part of the arms and neck. They became dusky red, and small, bright or dark red capillary punctae developed in each lesion and appeared like grains of cayenne pepper. These red points were more marked in some lesions than in others. The eruption at its onset was accompanied by a marked stinging or pricking sensation. After ten days the eruption faded, only to be followed in several weeks by a recurrence. The eruption had recurred every few weeks during the past four years, and the patient had had as many as eight attacks in two months. The lesions measured from 2 to 5 cm. in diameter; some were discrete, rounded, smooth and without infiltration, while others were confluent and formed irregular palm-sized patches. They left a brownish stain when they subsided. Numerous whitish, atrophic areas from 5 to 8 mm. in diameter were noticed on the anterior part of the forearms. Trauma was sometimes followed by hemorrhagic bullae. Small, flat, subcorneal vesicles containing serum were noted on the back of the right hand, measuring about 3 mm. in diameter. About twenty-five irregular subcutaneous nodules, round or oval and from 2 to 4 cm. in diameter, were palpable on the outer, upper part of the arms, chest, epigastric area and thighs, and had been present for five years. These nodules (lipomas?) were slightly tender and began one year before the appearance of the eruption. The palms, soles, face and scalp were free. The vertex of the scalp presented an almost complete alopecia, which the patient covered with a dark brown toupée. He complained of constant tender-

ness in the right iliac region. He gave a history of taking laxatives containing phenolphthalein at varying intervals, but he felt that he did not take this medicine sufficiently often to produce the eruption.

DISCUSSION

DR. HOWARD T. PHILLIPS: I believe that this case was one of phenolphthalein eruption. The patient gave a history of taking petrolagar from the bottle with a red label diagonally across it just before the last eruption appeared.

DR. J. J. HECHT: This patient gave a history of taking an oil similar to agarol or petrolagar, perhaps containing phenolphthalein. The condition looked like a phenolphthalein eruption to me.

DR. L. G. BEINHAUER: I agreed with the diagnosis as presented. The patient stated that five days previous to the onset of the present eruption he had taken a mineral oil containing phenolphthalein. The various stages of the lesions, the onset, the brilliant color and the symmetrical distribution favored the diagnosis of a drug eruption.

DR. CLAUDE B. NORRIS: To my mind the condition was undoubtedly a drug eruption, and phenolphthalein seemed to be responsible. We have here demonstrated very well one of the most peculiar difficulties with which one is so often confronted. The patient undoubtedly was a fairly intelligent man, and yet after several minutes of questioning I failed to elicit the admission that he had taken any drug. This shows how essential it is to exhaust every effort to get at the facts when one's suspicions are justifiably aroused.

DR. STANLEY CRAWFORD: I felt that the most likely cause of the present eruption was phenolphthalein, although it was difficult to get the patient to admit the various forms in which he may have taken it. I was unable to account for the small atrophic areas on the forearms, but I thought the subcutaneous nodules were probably lipomas.

A CASE FOR DIAGNOSIS. Presented by DR. L. G. BEINHAUER.

L. M., aged 3 years, consulted me for an eruption that began in December, 1931, with symmetrical, acute, inflammatory, nodular lesions, involving the right thigh, both elbows, knees, hands and fingers. The parents stated that the older lesions, such as those on the right flank, knee and hand, gradually subsided without treatment, and left a bluish stain. The patient had been taking medication given by the family physician for recurrent laryngitis and had been a "heavy eater" of Morton's iodized salt for the past year.

Examination revealed a well nourished infant, who presented an eruption involving the right flank, both aspects of the knee, the elbows, the dorsum of the right hand, the middle finger of the left hand and the right instep. The older lesions on the right thigh and both aspects of the knees apparently were involuting, leaving a dusky purplish discoloration which followed desquamation. The newer lesions on the hands, fingers and instep were firm, nodular, a shiny rose-red, freely movable in the skin and somewhat painful. Pressure apparently increased the size of the lesion, as one noticed over the right instep and left middle finger. The largest lesion on the right instep was about 2 cm. wide, while the smallest on the dorsum of the right hand was the size of a small pea. There was also an associated infection of the hair follicles of the margin of the eyelid. No laboratory examinations had been made.

DISCUSSION

DR. HOWARD T. PHILLIPS: I believe that this case was an early xanthomatous lesion, which will later resolve, with the typical yellow lesions of xanthoma tuberosum multiplex.

DR. STANLEY CRAWFORD: I consider that the red semiglobular lesions were an iodide eruption.

DR. H. G. WERTHEIMER: Though at first it seemed rather difficult to make a diagnosis, I favor that of ioderma. The color of the nodules, the painfulness and the history of taking iodides seem to support the diagnosis of ioderma.

DR. L. G. BEINHAUER: I am glad the consensus favors the diagnosis of an iodide eruption. I shall bear in mind the possibility of xanthoma, and shall report at a later meeting the progress of the patient.

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## BRONX DERMATOLOGICAL SOCIETY

THEODORE ROSENTHAL, M.D., *Secretary*

*Regular Meeting, Jan. 21, 1932*

HENRY SILVER, M.D., *President, in the Chair*

LUPUS ERYTHEMATOSUS AND LICHEN PLANUS. Presented by DR. SAMUEL FELDMAN.

J. McQ., a man, aged 47, a steamfitter, had received a severe sunburn the September prior to presentation. When that dermatitis wore off, the present condition remained. There was no other sensation outside of a slight itching and smarting on the forearms.

The patient presented three erythematous patches, on both cheeks and on the nose. Telangiectasia was visible in the areas involved. On the forearms there were two large symmetrically placed patches, violaceous and covered with scales. On the borders of these patches were a number of lichenoid papules. There were grayish papules on the buccal mucosa. The lips were covered with gray and scaly lesions. A section of tissue from the border of the areas on the forearm taken for biopsy revealed round cell infiltration in the upper and middle layers of the cutis and a large lake above the infiltration. The basal layer had disappeared, and the granular layer had markedly increased.

DISCUSSION

DR. A. ROSTENBERG: The lesions on the face and on the lips are typical of lupus erythematosus. The condition on the hands, however, does not permit of a definite diagnosis, but rather than assume two diseases, it would appear that the entire process is lupus erythematosus.

DR. F. A. DIASIO: The condition on the face is lupus erythematosus. I cannnot, however, diagnose the lesions on the hands as the chemical irritation has altered the process.

DR. I. M. LASHINSKY: We know that following injections of a gold preparation patients will frequently display erythematous lesions similar to those found on the forearms, and this may account for the process in this case.

DR. S. FELDMAN: The lichen-like lesions were situated on the borders of the erythematous area. Clinically, they were lichen planus papules, and this was confirmed by the biopsy. Moreover, the condition was decidedly not lupus erythematosus, for there was no collagen or degeneration of the elastic tissue. It is most unfortunate that a caustic was used, which to an extent destroyed the clinical appearance.

A Case for Diagnosis. Presented by Dr. Adolph Rostenberg.

Mrs. W., aged 66, gave an irrelevant personal and family history. The present skin eruption began about two years before presentation, involving mainly the flexor surfaces of the forearms. The eruption at that time closely resembled lichen planus. After treatment with roentgen rays and alpine light, in addition to injections of mercuric salicylarsenate, the rash faded somewhat, but did not disappear. In the course of time it spread slowly upward.

On examination, an eruption that started at the wrists and reached to the elbows, restricted markedly to the flexor surfaces, was found. The lesions consisted of bright red and dusky colored punctae which were closely aggregated and had a somewhat reticulated arrangement. There was total absence of itching or any other subjective symptom. Over both ankles were small areas somewhat suggesting the same condition.

DISCUSSION

Dr. A. Rostenberg: I have treated this patient for the last two years for lichen planus, without improvement. On the contrary the condition appears to be getting worse. The patient has had no itching at any time. The lesions are not typical, since they are darker in colors and punctate.

Dr. G. Spinner: I believe this to be a case of lichen planus. Since the lesions are in a senile skin, they give this peculiar clinical appearance.

Dr. C. Greenhouse: The lesions on the arm and the body are lichen planus, while those on the lower extremities impress me as being dermatitis hemostatica.

A Case for Diagnosis. Presented by Dr. Isidor Mogil.

P. L., a woman, aged 34, married and a mother, came to the clinic one week before presentation with an erythematous eruption, irregular in shape and sharply outlined, located on the shaft of the left leg near the ankle joint, which was very itchy and scaly at times. There were also rounded patches of a bluish-red color with a rough surface. These were not so itchy, but were somewhat scaly. They were paler in the center and were located on the trunk and at the waistline. The disease was of four years' duration, and began immediately following the birth of the patient's last child. So far, the eruption had not yielded to local treatment.

DISCUSSION

Dr. M. Kampf: The lesions on the leg resemble psoriasis.

Dr. C. Greenhouse: To me, the eruption looks like psoriasis that had been treated.

Dr. M. Umansky: I would suggest a diagnosis of neurodermatitis for the lesions on the leg, although those on the back do not fit into this picture.

Acne Varioliformis. Presented by Dr. Louis Chargin.

Mrs. R. B., aged 29, Russian by birth, a housewife, the mother of several healthy children, had an irrelevant personal history.

At intervals during the eight years prior to presentation, she had had a disease of the skin which tended to limit itself to the forehead at the hairy border, to the scalp and to the sides of the face in front of the ears. Small nodular lesions appeared which seemed to be fairly deep at the outset. These gradually became crusted, ulcerated and left superficial and deep scars which were quite round. The disease was particularly active during the winter months. It seemed to be aggravated during the menstrual period, and was never present during pregnancy.

The Wassermann test was negative. The tuberculin test, 1:10,000 and 1:1,000, was negative. At the time of presentation the patient exhibited numerous small and larger, active lesions in the sites mentioned and the remains of former

lesions in the form of scars. She had been treated with the usual remedies, including arsenic internally, with indifferent success. Suggestions for therapy were solicited. A biopsy confirmed the clinical diagnosis of acne varioliformis.

DISCUSSION

DR. S. FELDMAN: The history in this case is most interesting. In view of the fact that the patient is free from lesions during her periods of pregnancy, the case should be studied from an endocrine standpoint. I would use ammoniated mercury, U. S. P., externally and perhaps give the patient some roentgen treatment.

DR. C. GREENHOUSE: In England dermatologists have been giving lipoidal bismuth in cases of lupus vulgaris, and since it is believed that acne varioliformis has a tuberculous origin, perhaps injections of iodized oil and bismuth might be tried.

DR. T. ROSENTHAL: I would advise organotherapy.

DR. I. M. LASHINSKY: Perhaps some therapy with a gold preparation might be tried.

DR. C. LERNER: I would suggest injections of serum from a pregnant woman.

DR. L. CHARGIN: My original concept has been that acne varioliformis was a tuberculid. Since then I have altered my opinion, namely, that there are two types of acne varioliformis, one with a relationship to tuberculosis and one without. It is my belief that the type that is not related to tuberculosis responds to ammoniated mercury, U. S. P., whereas the other does not. I have already employed this locally as well as mercuric sulphide ointment. The treatment was not successful. I should hesitate to use therapy with a gold preparation or arsphenamine because of the possible dangers involved.

DERMATITIS EXFOLIATIVA. Presented by DR. SAMUEL FELDMAN.

A white man, aged 65, presented a scaly erythematous eruption over the entire body, the skin being covered with large lamellate scales which were easily detached. Those on the forehead, palms and soles were thicker and more firmly adherent.

Following the ingestion of cinchophen two and one-half years before presentation, a diffuse rash had developed that lasted only a few weeks. The patient had taken bromides for one and one-half years for a cardiac condition, until last July when a papular eruption developed on the arms, which rapidly spread over the entire body. Two months later, he entered Mount Sinai Hospital, where he was treated for eight weeks. He was discharged on Jan. 7, 1932, much improved. Two weeks later he entered Morrisania City Hospital. Besides the dermatologic picture, he presented arteriosclerosis, coronary sclerosis and prostatic hypertrophy.

Routine examination of the urine showed only traces of albumin. The Wassermann test was negative, and the white cell count was 9,500.

The patient was improving under local treatment with zinc stearate in oil and sodium thiosulphate, 7½ grains (0.49 Gm.) intravenously and 15 grains (0.96 Gm.) by mouth each day.

DISCUSSION

DR. COHEN: The patient gave a history of the ingestion of cinchophen. In the manufacture of cinchophen, arsenic is present as an impurity. Perhaps this arsenic has been the etiologic factor in this man's erythrodermia.

DR. S. FELDMAN: Urinalysis on several occasions failed to reveal arsenic. There was no history of psoriasis. The patient has received several injections of sodium thiosulphate with apparent benefit.

ERYTHEMA NODOSUM. Presented by DR. ADOLPH ROSTENBERG.

S. A., aged 51, first seen in 1927, stated that he had had previous attacks of the same trouble. At that time he presented an area about 5 by 4 inches (12.7 by

10.16 cm.) over the left tibia, which was reddish, infiltrated and very sensitive to the touch. The diagnosis was erythema nodosum.

On Jan. 16, 1932, the patient presented himself again with a lesion on the back of the right hand, which, he claimed, appeared and disappeared at regular intervals in this location. The lesions were bluish and irregular and did not disappear on pressure. There was a slight infiltration, especially in the periphery, where there were some small papules of a brighter reddish color. The patient did not complain of rheumatism or any other constitutional disturbance.

DISCUSSION

DR. C. GREENHOUSE: In view of the asymmetry, it is my impression that the lesions are due to tertiary syphilis.

DR. A. ROSTENBERG: The Wasserman reaction is negative, and I still feel that the process is erythema nodosum.

TUBERCULOSIS VERRUCOSA CUTIS. Presented by DR. GEORGE J. SPINNER.

W. T., aged 62, struck the back of his hand about nine months before presentation while cleaning a pipe of a sink. A papule formed which kept growing and became verrucous.

At the present time there is on the back of the left hand an elevated lesion 2 by 1½ inches (5 by 3.8 cm.), sharply marginated and showing typical verrucous growth. The Wassermann reaction of the blood was negative. Biopsy confirmed the diagnosis.

DISCUSSION

DR. H. SILVER: The lesions in this patient are much too flat to enable one to make the clinical diagnosis of tuberculosis verrucosa cutis.

DR. A. ROSTENBERG: I believe that this is a typical case, and agree with the diagnosis of the presenter.

DR. G. J. SPINNER: Histologic examination confirmed the diagnosis in this case. It seems that the lesions flattened after the section of tissue was taken for biopsy.

KAPOSI'S SARCOMA. Presented by DR. SAMUEL FELDMAN.

J. P., aged 45, employed by the department of sanitation, one year before presentation noticed small reddish papules in the groin. He was referred to a hospital for roentgen treatments, and he received thirty. At presentation the whole region of the groin was covered with infiltrated lesions, ranging in color from dark red to almost black. There were no lesions on the extremities, but the patient had acromegalic hands. There were two nodules on the cheek.

DISCUSSION

DR. C. LERNER: I agree with the diagnosis, but I am surprised at not finding any lesions on the feet.

DR. S. FELDMAN: Although the location is unusual, I believe that this condition is Kaposi's sarcoma. The results of histologic examination will be reported soon.

A CASE FOR DIAGNOSIS (ARSPHENAMINE ERUPTION, FIXED TYPE?). Presented by DR. I. M. LASHINSKY.

A. A., aged 29, single, born in Norway, came to the Mount Sinai clinic on March 3, 1931, requesting a Wassermann test. The patient gave a syphilitic history. Thirteen years previously he had an eruption for which he received twelve intramuscular and two intravenous injections. He had received no further treat-

ment. The result of the Wassermann test, made in March, 1931, was 3+. Since then, he had received two and one-half courses of treatment consisting of twenty injections of arsphenamine and thirty of bismuth.

About November 15, the patient noticed an eruption on both thighs consisting of from 10 to 15 mm. areas, bluish red, flat and mildly pruriginous. The eruption was not regarded as due to the treatment, and further injections were continued without any apparent aggravation of the eruption. Since the lesions bore some resemblance to a fixed eruption, further treatment with arsphenamine was given, but no local reaction was noted.

DISCUSSION

DR. R. BREAKSTONE: The color and general distribution of these lesions make me think that we are dealing here with a phenolphthalein eruption. The patient has admitted taking laxatives containing phenolphthalein.

DR. H. SILVER: I should like to call attention to the fact that phenolphthalein has been given to this patient without having produced an exacerbation of the lesions.

DR. C. GREENHOUSE: The administration of phenolphthalein need not necessarily light up the eruption even though it was originally due to the drug.

DR. M. UMANSKY: If this eruption is due either to phenolphthalein or arsphenamine, it should flare up following the administration of the offending drug.

DR. C. LERNER: My impression of the case is that we are dealing with either a trichophytosis or trichophytid.

DR. I. LASHINSKY: The outlines of the individual lesions do not resemble either trichophytosis or trichophytid. A biopsy was made to eliminate the remote possibility of a sarcoid, which was suggested. The important question I believe is this, "Are we dealing with a fixed eruption due to phenolphthalein or arsphenamine?" If so, lighting up of the lesions should be noted on administration of the respective drugs.

ALOPECIA TOTALIS. Presented by DR. MAX KAMF.

J. T., a girl, aged 18, whose illness began one month before presentation, first complained of an earache followed by vertigo and headache. This was followed by a loss of hair from the entire head. At the time of presentation she still suffered from general headache, which was worse at the vertex.

DISCUSSION

DR. F. A. DIASIO: The persistant headache, which plays a prominent part in the symptomatology of this patient, leads me to think of the possibility of an intoxication caused by thallium, which is contained in certain depilatory creams. I feel that this possibility should be eliminated.

DR. C. LERNER: I do not believe that this patient has alopecia totalis, because there are areas on the scalp that appear to have been shaved. I would say that the patient had a 50 per cent loss of hair and that the condition is alopecia areata.

DR. A. ROSTENBERG: The important question in this case is the matter of therapy. I am against pituitary therapy, because I fear that this method, indiscriminately used, will breed a new type of quackery. Sodium thiosulphate has been tried and occasionally yields good results.

DR. M. BERKOVSKY: Recently, I treated a patient with a similar case to whom two injections of solution of anterior pituitary and one of solution of posterior pituitary were given each week in addition to pituitary extract by mouth. In six weeks a good head of hair had grown.

DR. T. ROSENTHAL: A case of this type requires intensive investigation. First, metallic intoxications, such as lead and arsenic, must be eliminated, the

chemistry of the blood should be studied, basal metabolism determinations made and the endocrine status of the patient determined. With these factors known, we may hope to advance our knowledge of this distressing disturbance.

DR. L. CHARGIN: I believe that pituitary therapy should be given a fair trial. My only objection to it is that the administration of massive doses of a potent drug such as solution of pituitary may be theoretically harmful.

DR. S. FELDMAN: I have seen one patient who was given pituitary treatment for three weeks, and the condition has shown remarkable improvement.

DR. H. SILVER: I do not think that it is fair to attack this method of therapy without giving it a fair trial. In view of the favorable reports on pituitary therapy, as introduced by Bengtson, and the general interest in the subject, I have subjected half a dozen patients to this therapy. They were studied from an endocrinologic point of view, and the basal metabolism was determined in every case. The results so far are encouraging.

DR. M. KAMPF: This patient has been receiving solution of anterior pituitary by mouth. She presents definite signs of a pituitary dysfunction.

ERYTHRODERMIE CONGENITALE ICHTHYOSIFORME. Presented by DR. I. M. LASHINSKY.

B. S., a woman aged 50, married, born in Russia, came to the clinic on Jan. 13, 1932, complaining of itching all over the body. She was a well nourished person who had previously suffered from rheumatism and two years ago had had erysipelas. She had two healthy children living and had had two stillbirths. Urinalysis and the Wassermann reaction of the blood were negative.

The patient presented a thin, dry skin, covered with scales; between the scales were red lines. This condiion was most marked over the extremities. There was hypertrophy of the toe-nails; this condition had existed since her birth. There were keratosis of the palms and hyperkeratosis of the soles. Scattered irregularly were papules from 1 to 5 mm. in diameter which apparently caused the itching, so that the patient had a dermatitis superimposed on the general ichthyotic condition. The dermatitis disappeared after a few applications of sulphurated zinc paste, as did some of the scales. The patient said that her daughter was suffering from the same condition.

DISCUSSION

DR. A. ROSTENBERG: I do not agree with the diagnosis. We have here what is essentially an atrophy of the skin with the veins shining through. I believe that this is an early acrodermatitis chronica atrophicans.

DR. L. CHARGIN: There is considerable confusion regarding congenital ichthyosiform conditions with erythema. There are at present three separate types: (1) that in which the patient is born normal and in which ichthyosis develops after six months; (2) congenital ichthyosis with redness, in which the patient has a red face and arms, and (3) (*a*) ichthyosis gravis, in which the child is born dead or dies soon after birth, (*b*) ichthyosis lavata, in which the condition is not as serious as that just mentioned and (*c*) ichthyosis tarda, which develops later in life. I do not believe that this is a case of erythrodermie congenitale ichthyosiforme.

DR. S. FELDMAN: There is a certain amount of redness in both extremities, and the keratosis of the palms and soles and dystrophy of the toe-nails incline me to agree with the diagnosis.

DR. I. M. LASHINSKY: This case is not a typical example of the condition. McKee and Rosen have described cases like this in which there were bullae. In the ordinary type of ichthyosis one does not usually see keratosis palmaris et plantaris.

## CLEVELAND DERMATOLOGICAL SOCIETY

J. R. DRIVER, M.D., *Reporter*

*Regular Meeting, Jan. 28, 1932*

H. J. PARKHURST, M.D., *Presiding*

LYMPHOGRANULOMA INGUINALE WITH ANORECTAL SYNDROME (POSITIVE FREI TEST) TERTIARY SYPHILIS (CEREBROSPINAL). Presented by DR. HENRY DE WOLF.

F. M., a white woman, aged 35, from the Service of Drs. Cole and Driver at the Cleveland City Hospital, in November, 1930, had pneumonia, and at the same time had a rectal abscess, which healed in about a month. About Oct. 1, 1931, anal fistulas developed. Defecation became extremely painful. The condition became progressively worse, and the patient was admitted to the surgical service of the City Hospital on Dec. 28, 1931. She gave no history of primary or secondary lesions of syphilis, of venereal disease or of inguinal glandular disease. Two children were born dead. There was no history of miscarriages. She has been married twice. The first husband died of pneumonia; the physical condition of the second husband is fair, but he has not been examined.

The patient is a fairly well nourished white woman, not acutely ill. The pupils are irregular, unequal and rigid to light. Reflexes are physiologic. General examination otherwise showed nothing remarkable. Rectal examination revealed a high rectal stricture, a deep anal fissure and numerous fistulous tracts draining pus. Rectal examination is very painful. No deep induration can be detected by palpation. There is no enlargement of the inguinal glands and no lesion on the genitalia. The Wassermann reaction of the blood has been 4 plus on repeated tests. The spinal fluid shows 85 cells per cubic millimeter, a 4 plus Pandy reaction, a 4 plus Wassermann reaction, and a 5554321000 gum mastic curve. The Frei test has been strongly positive with two different antigens on two different occasions.

DISCUSSION

DR. J. VAN CLEVE: During the past year there have been, in the dermatologic service at the City Hospital twenty-four cases of lymphogranulomatosis inguinalis in which the diagnosis was proved by the Frei test. The woman presented here had a positive Wassermann test. In Europe a number of cases of stricture of the rectum have been reported in which the Wassermann test was positive. However, this is the first case that we have noted in our service. This patient has had no antisyphilitic treatment and she is now being given this type of treatment to see if it has any effect on the stricture.

DR. E. W. NETHERTON: I should like some one to outline briefly in more detail the course of the treatment.

DR. HENRY DE WOLF: There is no specific treatment for this disease. However, it is a specific venereal disease. There are many points in favor of this etiology. Two of the patients in this service have been treated with intramuscular injections of the prepared antigen used for the Frei test. My associates and I have not been much impressed with the results. Two patients have been treated surgically. I think that this will probably be the treatment of choice, provided operation is done before the formation of sinuses takes place. Roentgen therapy has been used extensively in European clinics, where it has been studied. We have also used it in our service, but I have not seen that it influences the course of the disease much. The difficulty is that the patients wait for several weeks after the onset before coming for advice; so, as a rule, the cases are not suitable for surgical intervention. We did try it in one case before the fistulas appeared.

The lesion was rather slow in healing, but the patient soon recovered the 15 or 20 pounds (7 to 9 Kg.) in weight that he had lost.

DR. J. R. DRIVER: Lymphogranulomatosis inguinalis is without any doubt a venereal disease, and it has been interesting to note, in the study of a rather large group of cases seen at the City Hospital, that all of these patients have been of the type that one encounters in dispensary practice. I have never seen one of these patients in private practice. The same is true of chancroidal infections, and it would seem that ordinary cleanliness probably suffices as a prophylactic measure against the infection, as in chancroidal infections.

DR. CLYDE L. CUMMER: Two or three cases have been seen at the Charity Hospital that I think fall into this class.

DR. C. G. LA ROCCO: I should like to ask Dr. De Wolf what he means by surgery-incision and drainage, or removal?

DR. HENRY DE WOLF: The involved glands should be removed. In the two patients in our service on whom we had operated fortunately there was no involvement of the iliac glands. When this occurs the operation is much more difficult. In the two cases cited merely the superficial glands were involved.

DR. E. W. NETHERTON: Is the disease common in women?

DR. HENRY DE WOLF: Recently there was a woman in our service with a typical picture of lymphogranulomatosis inguinalis. Unfortunately we were not able to study her carefully because her husband insisted on taking her home. The husband had a penile lesion and went to the Lakeside Hospital Dispensary. However, he would not permit us to examine him here, in spite of all our entreaties. The case presented in which the diagnosis was confirmed by the Frei test resembles those seen in men.

INFECTIOUS ECZEMATOID DERMATITIS. Presented by DR. HENRY DE WOLF.

A. L., a white man, aged 66, from the service of Drs. Cole and Driver at Cleveland City Hospital, has been in the hospital since July 18, 1931, suffering from a chronic pruritic disease. He has been shown at two previous meetings of this society (September and October, 1931). His eruption started about eight months prior to admittance. It began in the groins and spread over the body in a short time. The dermatitis has always been extremely itchy. Many kinds of treatment were used, with no permanent help. All of the studies made, including urinalysis, blood counts, chemical examination of the blood, the Wassermann test and biopsy, failed to throw any light on the cause of the eruption. A roentgenologic diagnosis of duodenal ulcer has been established, but at the time of this report the patient has no gastro-intestinal complaints. Treatment has consisted of permanganate baths, applications of silver nitrate, ultraviolet radiation, roentgen therapy and applications of various soothing and mildly stimulating preparations. At the time of this report he shows much improvement. The skin shows marked pigmentation, and on the lower extremities there is a mild papulopustular dermatitis. The scalp, face and ears show a scaly dermatitis.

DISCUSSION

DR. H. N. COLE: At the time when he was presented first, several members of this society felt that the patient had a typical odor of pemphigus; so he is presented at this time.

DR. E. W. NETHERTON: I admit that I was wrong. I thought that the patient had pemphigus. He has some pustules now and I think that the condition is an infectious eczematoid dermatitis.

DR. R. E. BARNEY: I thing that, in view of the extent of the process, the thickening of the skin and the presence of definite small papules, some appearing to be subacute, one ought to keep in mind the possibility of the development of lymphoblastoma, even though the patient does not show any adenitis at this time. I might also add that the liver and spleen are not palpable.

A Case for Diagnosis (Ichthyosis?). Presented by Dr. Claude B. Norris.

G. M., a girl, aged 7 years, was first seen in June, 1926, at which time a diagnosis of eczematoid xeroderma was made. The entire cutaneous surface was dry, and over the face was an eczematous rash which was interpreted at that time as being of the nature of infantile eczema. Small doses of roentgen rays were given, and lubricating ointments were applied. As time went on the condition cleared, but there remained more or less dryness and frequent exacerbations of the excessive dryness. During two or three winters ultraviolet irradiation was given over the entire body in the home, but the dryness persisted. It was observed by the mother that omission of the rays was followed soon by complete clearing of the skin and restoration of the normal baby skin-like softness. A peculiarity of the condition is that this excessive dryness takes place rapidly following a period during which the skin is apparently normal. This happened preceeding the present outbreak, the skin having been clear for two years, during which time no ultraviolet irradiation was given. The present condition came on overnight within the week prior to presentation here, beginning on the hands. The mother's skin is more or less dry, but this pronounced condition is not present in any other member of the family, except in one sister who has a tendency to eczema but not to dryness. The general health of the patient seems to be excellent.

DISCUSSION

Dr. C. G. La Rocco: The condition in the case presented today, because of the dry skin, resembles ichthyosis, but the history somewhat refutes that opinion. As I understand the history, this condition has cleared up and the skin has felt and appeared practically normal and then the condition has recurred. It suggests the type of eczematous ichthyosis that is seen in children.

Dr. J. R. Driver: The mother of this child has a dry skin, though not as marked as in the child, and I believe the condition is simply ichthyosis with a tendency to irritation by external irritants—among them something that the patient came in contact with recently. The weather has been unusually mild this winter which could explain the fact that she has had no trouble until recently.

Dr. M. J. Gibans: The flexor surfaces are markedly involved. There is erythema under the arms and in the folds. I think that the condition is congenital ichthyosiform erythema.

Dr. H. N. Cole: I should like to agree with Dr. Giban's remarks. The palms and soles are much thickened, reddened and scaly, and there are irregular, erythematous, fine, scaly areas on the body. I think the condition is a mild type of erythrodermite ichthyosiforme congenitale of Brocq, the type without bullae.

Dr. Claude G. Norris: I gave no consideration to any other hypothesis than that of ichthyosis until the condition appeared as it has the week prior to this presentation. The patient went through last winter without any trouble. The palms and soles have never been thickened and red as they are now. The mother called me on the telephone a few days ago and said that the child's skin was in good condition. The next day she brought the child to me, with her hands thickened and showing a reddish appearance, which is more pronounced today. The rest of the condition has become worse in the last few days. I believe that the suggestion that Dr. Gibans made, and in which Dr. Cole concurred, is good.

A Case for Diagnosis (Granuloma Annulare?). Presented by Dr. Claude B. Norris.

J. K., a Jewish girl, aged 12, was first seen on Sept. 19, 1931, at which time she presented on the left side of the neck, just beneath the ears, two ringlike lesions, concentrically placed, of two years' duration. The lesions were slightly raised and reddish. They were diagnosed as erythema elevatum diutinum, or

granuloma annulare. Roentgen irradiation and arsenic were given in what was regarded as sufficient dosage and over a sufficient length of time to produce some evidence of change. The mother was of the opinion that the lesions were getting larger in diameter. To this belief, full concurrence is not given. Below the lesions described was an irregular patch that had the appearance of pigmentation or rather of tattooing with powder or sand. The patient reported that this was caused by a sun blister while he was playing on the beach and that sand was rubbed into the skin. Nearly all of this discoloration was removed by the application of keratolytic salves and of cresol, U. S. P.

DISCUSSION

DR. E. D. STEINBERG: I thought of the diagnosis of circumscribed scleroderma.

DR. CLYDE L. CUMMER: I should like to know which group of lesions Dr. Norris regards as the part involved.

DR. CLAUDE B. NORRIS: The lower lesion, i. e., that area peeled off, the patient thought was deposits of sand in a blistered area. This lesion presented a pigmented, dirty brownish, spotty picture. I applied 6 per cent salicylic acid ointment, and some of the discolored portion came off, but a more glistening area did not respond. Tricresol was tried without any effect. Instruments had been used at the birth of the child; the mother reported that there was considerable trouble, and that there were bruised places on the left side of the neck for several weeks. Whether that fact would modify anybody's opinion as to the diagnosis in this case, I do not know. I gave the child half an erythema dose of roentgen rays applied to the upper lesions, as there was slight elevation of the red annular rings. Another ring, which I had not seen before, was noticed by Dr. Fisher today below the others.

DR. J. EDGAR FISHER: I am convinced that the condition is not scleroderma modified by treatment. From the history of the upper lesions under treatment I should still agree with the diagnosis of granuloma annulare.

DR. E. W. NETHERTON: The lesion, as Dr. Fisher said, was treated. The process seemed to be superficial, and there seemed to be a central atrophy, whether due to treatment or not I do not know. The margins appeared slightly granular and scaly. I thought the condition might be a fungus infection, though lasting quite a while. I think, however, that it is scleroderma. I do not believe it is granuloma annulare.

DR. H. J. PARKHURST: The principal point made in the history was that the lower lesion showed severe sunburn while the patient was in Florida. This area appeared to me to be vitiligo.

DR. H. N. COLE: I thought that the lower lesion looked very much like vitiligo. The area above looked as if it might have been burned with a hot water bottle or hot applications. It resembles erythema ab igne in its marmoraceous appearance.

DR. CLYDE L. CUMMER: I think that the upper lesions might be stains from applications of oil of bergamot.

DR. E. D. STEINBERG: I did not intend to refer to the upper lesions—just below them is a new patch that would make one suspect scleroderma.

NEVUS UNIUS LATERALIS. Presented by DR. HENRY DE WOLF.

E. F., a white, man, aged 20, from the service of Drs. Cole and Driver at the Cleveland City Hospital, has had a long linear lesion on the right arm as long as he can remember. He has also had wartlike lesions on the right thumb and forefinger all his life, which have slowly increased in size. The linear lesion on the arm has also grown slowly. On the anterolateral surface of the right arm is a linear process which begins at the shoulder and gradually disappears on

the lower third of the right forearm. It is composed of small, brownish papules simulating verrucae. Similar lesions are present on the radial side of the right forefinger. These have been altered somewhat by treatment. There is a scar on the dorsal aspect of the right thumb over the first joint. The linear nevus of the upper extremity varies in width from about 1 inch (2.5 cm.) at its upper limit to about ¼ inch (0.6 cm.) at its lower limit. It is slightly elevated above the skin. On Dec. 3, 1931, the lesion on the dorsal aspect of the right thumb was destroyed with the cautery. On December 9, the lesions on and near the right forefinger were treated by electrocoagulation.

DISCUSSION

DR. HENRY DE WOLF: I showed this case for suggestions as to treatment. Unfortunately biopsy has not yet been performed. I wonder if carbon dioxide snow would be worth trying?

DR. E. D. STEINBERG: I have been treating a child 2½ years old who has similar lesions on the knee. I tried carbon dioxide snow and electric cautery. Then I used trichloracetic acid, giving daily applications.

DR. H. N. COLE: I do not think that carbon dioxide snow causes any improvement in linear nevi of this type. Sometimes surgical treatment will help if the lesion is in a favorable place so that the surgeon can remove the nevus and bring the edges together with clips. Sometimes after carbon dioxide snow and after electric cautery the nevus tends to recur. I am interested in trichloracetic acid. It might produce good results.

DR. H. J. PARKHURST: In Dr. Wise's office my associates and I used to apply trichloracetic acid with excellent results, making new applications any time after the crust formed, which usually took from ten days to two weeks. I think that this lesion would respond well to electric cautery, however.

DR. C. G. LA ROCCO: Experience has taught me that not infrequently keloids result where an acid is used. I think that surgical intervention is the method of choice.

DR. CLAUDE B. NORRIS: I once started to remove a birthmark on a woman by means of electrodesiccation. Something happened to the machine, so I turned to the electric cautery and finished the operation by this method. The part of the lesion treated with electrodesiccation took longer to heal, and there was a mild keloid. On the part treated with the electric cautery there was no keloid and the area healed properly, giving a good result.

TULAREMIA. Presented by DR. HENRY DE WOLF.

*History.*—A. S., a white man, aged 58, from the service of Drs. Cole and Driver at the Cleveland City Hospital, was admitted to the hospital on Jan. 5, 1932, complaining of sores on his right hand. About December 20, the patient had noticed seven papular lesions on the right hand, which increased in size and became painful. Three days later he had chills, and when he consulted his physician he was found to have a temperature of 38 C. (100.4 F.). The fever lasted for five days. The papules on the hand had become large, red and somewhat swollen. There was a yellowish discharge from the lesions. His physician treated the lesions by immersing them in a hot antiseptic solution. About one week after the appearance of the lesions on the hand the patient noticed that the glands at the elbow and in the axilla were becoming enlarged and painful. He had considerable headache. Two days previous to the onset of his illness he had been hunting and had cleaned five rabbits that day. He did not recall that he had injured his hand. The only other time when he cleaned rabbits this season was about Nov. 15, 1931.

On admission to the hospital on Jan. 5, 1932, the patient showed seven lesions on the right hand. One lesion was located at the base of the nail of the right thumb, one over the web between the right thumb and right forefinger, four

over the knuckles of the right hand and one near the wrist on the dorsal aspect of the hand on the ulnar side. The lesions were of uniform size, about 1 cm. in diameter. They were papular with necrotic centers. The right epitrochlear and right axillary glands were moderately enlarged, firm and slightly tender. There was mild fever, the temperature not exceeding 37.8 C. (100.2 F.), during the time spent in the hospital. The leukocyte count was 12,400. The Wassermann test of the blood was negative. The agglutination test for tularemia was positive (1:320). The patient was given symptomatic treatment and was discharged on Jan. 15, 1932, considerably improved. The sites of the lesions on the hand were still visible, and epitrochlear and axillary adenitis could still be detected.

DISCUSSION

DR. J. R. DRIVER: This case is interesting to me because it is the first one of tularemia that I have ever seen with multiple primary lesions. This type of the disease, I believe, is comparatively rare.

DR. HENRY DE WOLF: I had not seen this patient for a week. My diagnosis was based on what I saw a week before his presentation here. The cubital and axillary glands were larger today than a week ago. I shall not be surprised if the axillary glands break down and have to be treated surgically. The patient has no general symptoms at the present time.

A CASE OF HEMANGIOMA PRESENTED FOR THERAPEUTIC SUGGESTIONS. Presented by DR. J. EDGAR FISHER.

D. J., a white girl, aged 5 years, was first seen on Jan. 20, 1932. At birth the big toe of the right foot was red and enlarged. The mother thought that the redness was due to a burn caused from hot water. About one year before presentation the foot was treated by a physician, who injected hot water into the tissue, with no apparent improvement. At present the right toe and the medial palmar surface are enlarged, red and soft. Roentgenograms show that the right toe is larger than the left.

DISCUSSION

DR. J. EDGAR FISHER: My reason for presenting this case is that the history is unusual. The process started at birth, but in recent years the mother has had trouble in getting shoes for the child—she has to buy two pairs, one pair larger than the other. Two months prior to presentation a physician attempted to inject hot water. He made three injections with no results. Another physician thought he could cure the condition with radium seeds and subsequently an operation. I happened to see the child, and I told the mother I was going to present her before a group of physicians to see what they would suggest.

DR. H. N. COLE: I do not see how radium seeds could help. I am interested in the enlargement of the bones, which is probably due to the increased blood supply of the nevus. I should think that such a result would be possible. I do not know of anything that can be done. Perhaps surgical intervention can be employed; the redundent tissue can be removed, but that will not help the enlargement of the bones.

DR. R. E. BARNEY: I should leave the foot as it is. It is not causing trouble, and as long as the condition remains asymptomatic I should leave it alone.

TUBERCULOSIS VERRUCOSA CUTIS. Presented by DR. J. V. AMBLER.

J. R., a middle aged white man, a painter, from the service of Drs. Cole and Driver at the Lakeside Hospital, presented himself at the Lakeside Hospital Dispensary on Jan. 26, 1932, for treatment of a chronic eruption on the face of fifteen years' duration. The process had started fifteen years before as a small papule on the right cheek and had gradually spread at the border and cleared in the center. The patient has had no treatment except with local ointments.

He has been married for twenty-five years. His wife was pregnant once, twenty-four years before the patient's admission to the hospital, with a miscarriage at six months. She has pulmonary tuberculosis of twenty years' standing, which became quiescent but has become active again recently. The patient had a penile lesion thirty years prior to admission. His general health has been excellent.

The lesion was confined to the right side of the face, the active advancing border being along the hair line, anterior to the ear and down onto the lower part of the cheek. The border was serpiginous, verrucous and piled up, with the extreme advancing edge dark red, smooth and shiny. As the lesions advanced superficial residual scars were left behind. Biopsy sections of skin and subcutaneous tissue were taken. The surface of the epidermis was irregular and covered by a thick layer of keratohyalin. The epithelial papillae were elongated, broad and of irregular contour. There was diffuse inflammatory change in the corium with focal areas of acidophilic granular necrosis and both focal and diffuse collections of epithelioid cells. There was diffuse infiltration of lymphocytes and occasional giant cells of the Langhans type.

DISCUSSION

DR. J. E. RAUSCHKOLB: I was wondering about the possibility of a superficial gumma, slow and insidious in onset and progress. The Wassermann test was negative, but there is a history of a lesion several years ago. The scar looks like a healed syphilitic process. The picture shows Langhans' type of giant cells.

DR. H. N. COLE: I think the process has in part the picture of a serpiginous type of lupus vulgaris and some of the other characteristics of tuberculosis verrucosus cutis. The histologic picture bears out this diagnosis. The lesion apparently is of a low grade with good immunity on the part of the patient; hence its slow spread at one border, with clearing at the other.

DR. J. V. AMBLER: I might add to the history that fifteen years before this presentation, when the lesion first started, the patient was presented before a class at Rush Medical School. He remembers that the professor said the disease was of the butterfly type which would spread across the nose. At that time apparently it was considered to be lupus erythematosus. A Wassermann test has been made, but the results have not been reported yet. The patient said that several Wassermann tests in the past had been negative.

DR. R. E. BARNEY: It is interesting in a case of tuberculosis to see so little scarring after fifteen years. There is one area near the ear that makes one think of tuberculosis verrucosus cutis of a superficial type.

A CASE FOR DIAGNOSIS. Presented by DR. J. EDGAR FISHER.

N. G., a woman, aged 20, is under treatment for acne vulgaris involving the face and back. In addition, she complains of always feeling cold. For a number of years she was in the habit of sitting near a radiator or open fireplace to keep warm. At present the legs show the typical eruption seen in erythema ab igne. For the past two months the disorder has appeared on the arms.

DISCUSSION

DR. J. E. RAUSCHKOLB: I believe this condition is a vasomotor disturbance primarily associated with a type of cutaneous eruption, livedo reticularis. Erythema ab igne has a brown or burnt color. The eruption in this case is bluish and blanches on pressure. Moreover, the disturbance is on the plantar surfaces of both feet.

DR. H. N. COLE: I agree with Dr. Rauschkolb that this condition is not exactly like erythema ab igne. It possibly belongs in the group of livedo reticularis, but more likely it comes under the group described by Parkes Weber of London (*Brit. J. Dermat.* **39**:259 [June] 1927). Weber reported two cases of a condition

that he entitled "A Chilblain Condition of the Legs, Somewhat Resembling Erythema Induratum." His cases were the counterpart of that of this patient, showing a type of marmoraceous acrocyanosis of the lower limbs. Weber felt that the condition was not uncommon in young girls and laid it to the present custom of lack of covering of the lower limbs. There is defective circulation in the superficial portion of the skin during the cold weather, resulting finally in this inflammatory type of reaction. Weber expressed the belief that the eruption develops on the lower limbs because of the poor return circulation in this area, and especially on account of the thin stockings that women are accustomed to wear. In a chlorotic type of young woman, with her hands as well as her legs exposed, I see no reason why the same condition could not develop on the backs of the hands, as is seen in this patient.

DR. C. G. LA ROCCO: This patient mentioned that when she gets warm the condition tends to disappear.

A CASE FOR DIAGNOSIS. Presented by DR. HENRY DE WOLF.

Dr. N. K., a white man, aged 26, an intern at the Cleveland City Hospital, from the service of Drs. Cole and Driver at this hospital, about three or four months prior to presentation noticed a small lesion on the left side of the forehead, which has increased slowly in size. It varies in its appearance from time to time. The color is much less bright after a night's rest, but becomes more evident on activity. There have been no subjective symptoms, and no medication has been applied to the lesion.

The lesion is located on the forehead, slightly to the left of the midline and about halfway between the hair margin of the scalp and the left eyebrow. It is roughly circular and about the size of a dime. It is moderately indurated and only slightly raised. The periphery of the lesion is brighter than the central portion. No laboratory studies have yet been made.

DISCUSSION

DR. C. G. LA ROCCO: On first inspection the condition suggested the possibility of lupus erythematosus, but on more careful examination it does not show telangiectasia or scars. I was under the impression that the condition might be some form of drug eruption.

DR. M. J. GIBANS: I agree with the diagnosis of drug eruption. I know a musician who presents an identical picture on the forehead after drinking beer. If the two eruptions were photographed, one could not tell one from the other.

DR. H. N. COLE: I think there is a possibility that the condition might be a beginning sarcoid of Boeck. It would be a good plan to take a specimen to see what it would show. The process is indolent and reddish brown and has lasted for a long time with no tendency to break down.

DR. HENRY DE WOLF: My impression of this lesion was first that it was a sarcoid. I have had no opportunity to investigate it, but I think the patient's physician would be willing to let a biopsy specimen be taken in order that a diagnosis may be made. At the next meeting I shall report what is learned.

# Directory of Dermatologic Societies *

## FOREIGN

### British Association of Dermatology and Syphilology (Canadian Branch)

Philip Burnett, President, 2 Simpson St., Montreal.
L. P. Ereaux, Secretary, 1380 Sherbrooke West, Montreal.

### Royal Society of Medicine, Section of Dermatology

President: A. M. H. Gray, 30 New Cavendish St., W. 1, London.
Secretary: H. Thompson Barron, 53 Queen Anne St., W. 1, London.

## NATIONAL DERMATOLOGIC SOCIETIES

### American Medical Association, Scientific Assembly, Section on Dermatology and Syphilology

Francis Eugene Senear, Chairman, 55 E. Washington St., Chicago.
Harry R. Foerster, Secretary, 759 N. Milwaukee St., Milwaukee.
Place: Milwaukee. Time: 1933.

### American Dermatological Association

Fred Wise, President, 200 W. 59th St., New York.
W. H. Guy, Secretary, 7026 Jenkins Arcade, Pittsburgh.
Place: Chicago. Time: 1933.

## SECTIONAL DERMATOLOGIC SOCIETIES

### Baltimore-Washington Dermatological Society

Lee McCarthy, President, 1835 Eye St. N. W., Washington, D. C.
M. H. Goodman, Secretary, 401 Medical Arts Bldg., Baltimore.

### Central States Dermatological Association

Howard J. Parkhurst, President, 316 Michigan St., Toledo, Ohio.
Robert E. Barney, Secretary, 1021 Prospect Ave., Cleveland.
Place: Pittsburgh. Time: October, 1932.

### Iowa and Western Illinois Dermatological Association

J. C. Kessler, President, University Hospital, Iowa City, Iowa.
Robert E. Jameson, Secretary, 201 West Second St., Davenport, Iowa.

### New England Dermatological Society

Arthur M. Greenwood, President, 416 Marlboro St., Boston.
William P. Boardman, Secretary, 388 Marlboro St., Boston.

### Southern Medical Association, Section on Dermatology

Emmet R. Hall, Chairman, 1001 Exchange Bldg., Memphis, Tenn.
Dudley C. Smith, Secretary, University, Va.

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* Secretaries of dermatologic societies are requested to furnish the information necessary for the editor to make this list complete and to keep it up to date.

## STATE DERMATOLOGIC SOCIETIES

### Florida Society of Dermatology and Syphilology

Chairman for each meeting is elected from city in which meeting is held.
Frank Wilson, Secretary, 310 Greenleaf & Crosby Bldg., Jacksonville, Fla.
Place: Jacksonville, Tampa, Miami and place of meeting of state medical society.
Time: Quarterly.

### Louisiana Dermatological Society

R. A. Oriol, President, 921 Canal St., New Orleans.
M. T. Van Studdiford, Secretary-Treasurer, 150 Baronne St., New Orleans.

### Medical Society of the State of New York, Section on Dermatology and Syphilology

Edward R. Maloney, Chairman, 853 7th Ave., New York.
George C. Andrews, Secretary, 115 E. 61st St., New York.

### Medical Society of the State of Pennsylvania Section on Dermatology

Edward F. Corson, President, Medical Arts Bldg., Philadelphia.
Stanley Crawford, Secretary, 200, 9th St., Pittsburgh.

### Michigan State Medical Society, Section on Dermatology and Syphilology

Cyril K. Valade, Chairman, 1604 Eaton Tower, Detroit.
George H. Belote, Secretary, University Hospital, Ann Arbor.

### Minnesota Dermatological Society

H. N. Klein, President, 350 St. Peter St., St. Paul.
D. D. Turnacliff, Secretary, 407 Medical Arts Bldg., Minneapolis.

### Oklahoma Dermatological Association

C. J. Woods, President, 108 W. 6th St., Tulsa.
C. L. Brundage, Secretary, 616 Medical Arts Bldg., Oklahoma City.

### Texas Dermatological Society

N. Riley Jackson, President, 110 W. 7th St., Austin.
Everett R. Seale, Secretary, 1215 Walker Ave., Houston.

## LOCAL DERMATOLOGIC SOCIETIES

### Atlanta Dermatological Society

Francis G. Jones, President, 384 Peachtree St., Atlanta, Ga.
Charles A. Wilkins, Secretary, Medical Arts Bldg., Atlanta, Ga.

### Bronx Dermatological Society

Henry Silver, Chairman, 290 West End Ave., New York.
Theodore Rosenthal, Secretary-Treasurer, 115 W. 86th St., New York.

### Brooklyn Dermatological Society

B. B. Berkowitz, President, 225 Eastern Parkway, Brooklyn.
A. M. Persky, Secretary, 1750 Ocean Pkwy., Brooklyn.

### Chicago Dermatological Society

Michael Ebert, President, 25 E. Washington St., Chicago.
E. A. Oliver, Secretary, 55 E. Washington St., Chicago.

### Cincinnati Dermatological Society

H. Jerry Lavender, President, 716 Provident Bank Bldg., Cincinnati.
Raymond G. Senour, Secretary-Treasurer, 19 W. 7th St., Cincinnati.

### Cleveland Dermatological Society

Howard J. Parkhurst, President, 316 Michigan St., Toledo.
Robert E. Barney, Secretary, 1021 Prospect Ave., Cleveland.

### Detroit Dermatological Society

Claud W. Behn, President, 1546 David Whitney Bldg., Detroit.
William G. Saunders, Secretary-Treasurer, 9203 Grand River Ave., Detroit.

### Los Angeles Dermatological Society

Irving R. Bancroft, Chairman, 412 W. 6th St., Los Angeles.
Chris R. Halloran, Secretary, 1052 W. 6th St., Los Angeles.

### Manhattan Dermatologic Society

Fred Wise, Chairman, 200 West Fifty-Ninth St., New York.
Mihran B. Parounagian, Secretary, 126 E. 39th St., New York.

### Montreal Dermatological Society

J. F. Burgess, President, Drummond Medical Bldg., Montreal, Canada.
B. Usher, Secretary-Treasurer, Medical Arts Bldg., Sherbrooke St., W., Montreal, Canada.

### New York Academy of Medicine, Section of Dermatology and Syphilis

Joseph J. Eller, Chairman, 100 W. 59th St., New York.
Leo Spiegel, Secretary, 241 W. 100th St., New York.

### New York Dermatological Society

John Frank Fraser, President, 100 W. 59th St., New York.
Edward R. Maloney, Secretary, 853 7th Ave., New York.

### Philadelphia Dermatological Society

Jacob M. Schildkraut, Chairman, 170 W. State St., Trenton, N. J.
Jacques P. Guequierre, Secretary, 1930 Chestnut St., Philadelphia.

### Pittsburgh Dermatological Society

J. H. Fiscus, Chairman, 121 N. Main St., Greensburg, Pa.
Claude B. Norris, Secretary, 244 Lincoln Ave., Youngstown, Ohio.
Place: Pittsburgh. Time: October, 1932.

### St. Louis Dermatological Society

Richard S. Weiss, President, 3720 Washington Blvd., St. Louis.
M. F. Engman, Jr., Secretary-Treasurer, 3720 Washington Blvd., St. Louis.

### San Francisco Dermatological Society

Charles Schoff, President, 1127, 11th St., Sacramento, Calif.
John M. Graves, Secretary, 909 Hyde St., San Francisco.